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Read this!! The information on this site is for experimental purposes only. There is no scientific proof that thyroid disease can be corrected nutritionally. The editor of this site is not a doctor and has no formal medical training. What works for one person may be dangerous for another. Consult a qualified nutritionist who knows your health condition before commencing any supplement program.

Search for:

New to the Site? Check out these areas:

- [Greetings from John--what this site is about.](#)
- [Think you might have thyroid disease?](#)
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- [Should you have RAI?](#)
- [Is the radio iodine uptake test \(RAIU\) dangerous?](#)
- [Talk about your experiences on the Bulletin Board.](#)

What's New at iThyroid?

- **10-15-05** Mary Shomon's new book is out with a lot of good information including a chapter on my nutritional protocol for correcting hyperthyroidism. Her book is called "Living well with Grave's Disease and Hyperthyroidism: What Your Doctor Doesn't Tell You...That You Need to Know."
- **10-21-01** [Balancing Calcium and Magnesium](#)---the key to avoiding irregular heart rate.
- **2-11-01** New page called "[Latest Ideas](#)" with new thoughts on potassium.
- **9-15-00** [Phthalates](#) and [DHEA](#). New information suggests that these hypolipidemic agents may promote hyperthyroidism.
- **8-13-00** [Boron](#): Studies show that boron is critical for magnesium and calcium metabolism, raises serum copper levels, increases estrogen and testosterone, and is probably very important for the control of thyroid disease, especially hyperthyroidism.
- **8-10-00** [Laboratory Tests for Thyroid Function](#) By Elaine A. Moore
- **6-14-00** [Chocolate](#)--High cadmium content makes it a negative for those with thyroid disease, despite the fact that it is high in copper.
- **6-1-00** [Cadmium Sources](#) in our food, air, and water. Book excerpt identifies many cadmium sources. A MUST read for everyone!!
- **5-25-00** Certain foods called tyramines, such as chocolate, wine, beer, and bananas can contribute to headaches, hypertension, and possibly hyperthyroidism in certain individuals. Take a look at [Tyramines, MAO and MAOI](#), in the new [Deeper Studies](#) section.
- **5-21-00** [Mercury](#) file rewritten. Mercury toxicity from dental fillings is a major health problem and a significant factor in thyroid disease and anemia. Mercury accumulation can be accelerated significantly by the consumption of milk and probably by estrogen.
- **5-5-00** ANEMIA is highly associated with thyroid disease. In fact, anemia may be the beginning of thyroid disease. Hyperthyroidism may be copper-deficiency anemia and hypothyroidism may be iron-deficiency anemia. [Click here to read about Anemia.](#)
- **5-5-00** New hypothesis why milk adversely affects hyperts: [MILK](#)
- **4-26-00** Don't get iron deficient! Read the story of how I got iron deficient so it doesn't happen to you. Click here: [Iron](#)
- **4-25-00** Read about [Cadmium](#). It appears that cadmium is a (or maybe the) prime cause of thyroid disease.
- **4-23-00** New section for hyperts: [Getting Started.](#)
- **4-21-00** Where to get a hair analysis. [Hair analysis.](#)
- New information on [Drinking Water.](#)
- New **4-14-00** [Medical Treatments for Graves'.](#)
- New **4-12-00** [Bone and Teeth Problems](#)

If you have thyroid disease, what should you do? Follow these steps:

1. **Don't get hurt.** Hyperthyroidism is dangerous and kills. Get to a doctor and get antithyroid medications to prevent heart failure. Be careful though. Many people get persuaded into undergoing RAI before becoming informed about the dangers. Educate yourself first. Read the section [RAI or not RAI?](#) If you have hypothyroidism, take replacement hormone. I've seen no evidence that not taking hormone will stimulate your thyroid to work harder. Nutrition may reverse the hypothyroidism, but until then take

hormone. Read about the hormone choices, Synthroid or Armour, on [HypoT Treatments](#).

2. **Explore the Section, "New to the Site?"** above.
3. **Become your own doctor.** *Don't put your life in someone else's hands because they don't care as much about you as you do. Don't trust anyone else, including me. Do your own research. This site is devoted to research into the nutritional basis of disease, but this work is experimental. Nothing you will read at this site or hear from anyone else has been proven to work 100% of the time. You have to find your own path.*
4. **Study.** *I've assembled a lot of information from observations from my own disease experiences, others experiences, and published scientific studies. The deeper you go into this site the more detailed information you'll find. Read the information here and then do your own research. You may discover something critically important that no one has found before.*
5. **Interact.** *Go to the bulletin board and tell your story and experiences. We all learn from those stories. When you find something that works for you report back to the group. We make progress by all helping each other.*
6. **Post your story.** *If you have success or failure following a particular strategy, write all the details down and send it to me BU007@aol.com for posting under the appropriate disease category. This way there will be a permanent record that everyone can refer to so that the story won't have to be told over and over.*

This site is for everyone.

While statistics tell us that about 5-10% of the population have or will get thyroid disease, my estimation is that at least 80% of the population has nutritional deficiencies that result in reduced mental and physical capacities and which could eventually lead to degenerative diseases like thyroid disease and other autoimmune diseases.

This site has health and nutritional information that is not available anywhere else. Dig in and I think you'll find the study of nutrition incredibly fascinating. You may find the nugget of information that will lead you to correct your disease condition. If you don't find it, ask on the bulletin board.

Confused by Nutrition?

Don't worry, everyone is confused. It's complicated. However, it's making more sense all the time.

Many people discount nutrition because of all the conflicting information. One day food X is found good for you; next day food X is found bad for you. What do you do? Give up or dig deeper? I dig deeper.

If people can nutritionally correct diseases which are not understood by mainstream medical practitioners like hyperthyroidism and hypothyroidism, then anything is possible.

In my opinion, If you have a disease, including the autoimmune diseases, it's probably due to a nutritional deficiency and can be corrected. Mainstream medicine isn't looking into the nutritional correction of these diseases, but here we are.

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Greetings from John:

Everyone with a thyroid disease wonders what is going on--How did I get this disease? Many people who get hyperthyroidism or Graves' disease are really surprised because they, like I, felt really great just before getting sick.

Even Olympic class athletes develop Graves' disease, making us all realize that if people in apparent top health and conditioning can get it, then anyone can.

After going through and recovering from both hyperthyroidism and hypothyroidism, I feel that I have a very good idea what causes these diseases and my theory is at odds with current medical thinking.

I believe that hyperthyroidism and hypothyroidism, Graves' disease and Hashimoto's Thyroiditis, are caused by a combination of nutritional deficiencies and chemical toxins, usually heavy metals.

I have had both hyperthyroidism and hypothyroidism and corrected both conditions through nutritional supplementation and I feel very strongly that I can show you how to do the same.

If you want to live with these diseases or switch from hyperthyroidism to hypothyroidism by getting RAI, then medical doctors can help you to do this. I really don't recommend this, because this approach does not improve your health but only pushes you down the path to more serious health problems.

However, if you want to correct these conditions by getting to the cause, then there is only one way--through nutrition. You can change your nutritional status by changing your diet and/or by adding or changing your nutritional supplement program.

If you want to stop your current downward trend in your health and start improving your health to minimize or eliminate these diseases from your life, then you're going to have to do a lot of work. You're going to have to take control of your life and become your own doctor, educate yourself about health and the essential nutrients that your body needs to maintain thyroid health, get to the store and buy the supplements and foods that will help you, maintain a diary so you know what's helping and what's hurting, and develop the determination not to give up. I and other people at this site will help you, so you're not on your own.

What's my motivation? I'm not out to sell you anything. Whatever supplements you need, you'll have to hunt them down and find them somewhere else. My motivations are simple: first, thyroid diseases have taken years of my life and I hate them and want to see them eliminated as much as possible from the world; and second, I can't stand to see people suffer from something that I feel I can help correct.

Thyroid diseases are not easy to correct but I believe it's possible. They are not simple, one-deficiency diseases, but are the result of complex and inter-related nutritional deficiencies and toxicities. Hyperthyroidism is particularly difficult because once you get it just about every nutritional supplement and many foods make the condition worse. It's very much like falling into quicksand--it seems no matter what you do, you just keep sinking deeper and deeper. I call it the "backward disease" because it defies standard nutritional logic and gets worse when you take the nutrients that usually help most disease conditions.

I've been in that hyperthyroid quicksand and just before my head went under, I figured out the right nutritional strategy and escaped. Fortunately I kept a diary and that diary has provided a roadmap to guide others out of that mess.

Hypothyroidism is a quagmire also. In hyperthyroidism you at least know that your thyroid is capable of producing hormone. The problem is how to find the brakes. In hypothyroidism you think your thyroid is broken and can never be repaired. I hope to show you that this isn't the case and the solution might be as simple as changing your diet, having your silver amalgam (mercury) dental fillings replaced, and taking nutritional supplements.

The biggest obstacle in overcoming thyroid disease is that the person's energy level and brain functioning are so low that it's extremely difficult to figure out what to do and to take the steps necessary to improve. Just about everyone with thyroid disease refers to this condition as "brain fog."

I've used nutrition for decades to correct my health problems, but when I had thyroid disease, my brain was barely working. Fortunately I had the time to study nutrition for the months on end that it took (because my brain functioning was low) and the sense to keep a diary so that I could analyze what nutrients were helping and what were hurting.

Once I started supplementing with the nutrients I needed to correct hyperthyroidism, the increase in brain function and energy level was amazing. I didn't realize how much of a fog I was in until I got out of it. I always say that getting hyperthyroidism was one of the worst experiences of my life, but recovering from it was one of the best. I can have the worst job to do like lying in the dirt under a car trying to fix it on a hot, sweaty summer day with bugs biting me and I'm still happy--happy to be alive and able to just do the job.

Thyroid disease is the result of the accumulation of many years of nutrient deficiencies. I think you'll find as I

did that once you correct those deficiencies, life is truly great!! You'll be amazed.

People with thyroid disease tend to flip back and forth between hypothyroidism and hyperthyroidism. Most people with hypothyroidism don't seem too concerned about their plight until it gets bad. They think, "Oh, I just take this little pill once a day and I'm fine." Please take my advice and start learning now. Hypothyroidism for many people is the first step toward hyperthyroidism. Believe me, you don't want to experience it. It's not the way to lose weight! If you have hypothyroidism and are overweight, let me show you a better way to correct those conditions. Even if hypothyroidism doesn't lead to hyperthyroidism, it's an indication that your health is poor and your energy is low. Learn what nutrients are deficient in hypothyroidism, correct those deficiencies, and feel the physical and mental differences that health can make in your life.

While there is a lot of information on this site to read, I would urge anyone with Graves', Hashimoto's, hyperthyroidism, hypothyroidism, or any other autoimmune disease, to study everything carefully so that you understand what pushes you hyper, what pushes you hypo, and what causes the immune system to go wacky in autoimmune disease. This information may protect you from getting into worse trouble.

On this site you can read about my background and stories of how I developed and recovered from hypothyroidism and hyperthyroidism.

Thyroid disease is primarily a disease of women. Close to 90% of the sufferers are female. The risk of getting Graves' Disease and Thyroid Eye Disease (TED) is greatly increased by smoking. Read my theory about why women are the victims, how smoking affects the thyroid and TED, and why women should never smoke, get silver amalgam (mercury) dental fillings, and should protect themselves from other heavy metal toxic sources.

You can read the latest version of the Thyroid Supplement List and details about how each nutrient affects the thyroid and endocrine system.

Also you can read my interpretation of the science of medicine versus the art of medicine and explore how we know anything and how sure we are of what we think we know.

This is an interactive site. I have had a group on Egroups.com since September, 1998, and everyone who has participated has learned an incredible amount by working together, trying the supplement program, and reporting back to the group on the results.

This is a group effort and many people have contributed and continue to contribute. I hope to develop additional features of the website including pages devoted to the interpretation of thyroid medical tests and the interpretation of hair mineral analyses. Hopefully other members will also contribute to these and other areas. If you have expertise in any related area or related disease conditions, please let me know so that we can add that information to the site.

This is your site so let me know what you would like to see. I wish you all the very best of health and pledge to do my best to provide you with the information and motivation to attain that.

*Sincerely, your friend,
John Johnson
BU007@aol.com*

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GETTING STARTED CORRECTING HYPERTHYROIDISM

Finding the Path

Finding the optimum path to correcting a disease, especially a complicated disease like thyroid disease, can be simple or challenging. While I have a pretty good concept of the deficiencies involved in Graves' Disease derived from my own experiences, others' experiences, studying hair analyses of people with Graves', and studying the scientific literature, there are individual differences.

For example, copper is a key mineral which seems always deficient at the cellular level in Graves', but some persons have low tissue and hair levels of copper and others have high hair levels and presumably have high levels of copper stored in their livers. A different plan of action has to be used for different conditions.

I have developed a theory for the correction of nutritional deficiency diseases and I believe that most diseases are nutritional deficiency diseases. Most diseases like diabetes, hypothyroidism, and hyperthyroidism, don't appear to be deficiency diseases because they involve very complex inter-related nutrient deficiencies. When medical scientists, medical practitioners, or individuals on their own attempt to correct these diseases with a single or limited group of nutrients, they condition invariably fails to respond and often gets worse. I have experienced this, seen it in others, and have a theory of why this happens.

Nutritional deficiency diseases which are very resistant to correction involve deficiencies of numerous nutrients. Some nutrients are very deficient while others are only somewhat deficient. Some nutrients are key nutrients and when they get deficient this causes other nutrients to be unusable by the body in certain metabolic pathways and therefore they take on toxic-like effects.

Nutrient Interactions

All nutrients and especially minerals need to be present in the body in the proper balance. When there is a pair of nutrients which work together and one of these nutrients gets deficient, ingestion of the other nutrient causes the less available nutrient to get used up and become even more deficient.

For example, copper and iron are key nutrients which are usually deficient in hyperthyroidism. Since copper and iron work together in many functions such as forming hemoglobin, the oxygen-carrying molecule in the red blood cells, a deficiency of copper can cause iron to become toxic to the body. When the person takes iron, which is in virtually every multiple vitamin/mineral supplement, without taking enough copper and most of these aforementioned supplements are deficient in copper, then the copper becomes more deficient and the person gets sicker.

Because iron and copper are both necessary for hemoglobin production, anemia can result from a deficiency of either nutrient. A person can have iron-deficiency anemia or copper-deficiency anemia. Doctors seem to be very aware of iron-deficiency anemia and not very aware of copper-deficiency anemia. I've seen more than one case where an anemic patient has been prescribed massive doses of iron (up to 200 mgs. per day) to correct anemia and the anemia has gotten worse. This high iron intake eventually caused a severe copper deficiency and the development of thyroid disease. When I convinced the person they were probably suffering from copper-deficiency anemia and they commenced copper supplementation, the anemic condition finally improved.

Because vitamins and minerals work together in pairs, the same type of interaction can occur when a vitamin is taken to excess and the mineral which the vitamin facilitates is not taken. For example, selenium and vitamin E work together and among many functions they protect the body from free radical damage and work to prevent cardiovascular damage which manifests as heart disease. Large scale studies that have looked at the effect of vitamin E on preventing heart disease have found results which were curious to the scientists. At levels of less than 200 IU of vitamin E a day there was more heart disease than at 400 IU per day. But persons who took 800 or more IU per day experienced a higher rate of heart disease than those taking 400 IU. The scientists were baffled because more of a good thing didn't produce more benefits. Why is this?

My theory is that because vitamin E does not work alone and is really just the facilitator for the real protector, selenium. Since selenium wasn't supplemented in the study, the vitamin E provided the maximum benefit at 400 IU. At 800 IU the vitamin E was actually causing selenium to be depleted so the protective effect was diminished.

This interaction is seen in many nutrient combinations. Vitamins which work with copper, such as B-1, B-2, B-3, and C, can deplete copper is taken in excess and copper is not supplemented. High intake of zinc can deplete copper and iron. High intake of cadmium can deplete zinc, copper, and probably silver. High manganese can deplete chromium. High sodium can deplete potassium and probably lithium. High calcium can deplete magnesium. The list goes on and on.

THEORY OF NUTRITIONAL CORRECTION

This brings me to my theory of correcting nutritional deficiency diseases: *You have to start with the most deficient nutrient.* If you begin supplementation with anything but the most deficient nutrient, then this nutrient will get more depleted and the disease condition will worsen.

When I had hyperthyroidism and was experimenting with taking different nutrients, it seemed that everything I tried made it worse. Several nutritional books and my nutritionist doctor recommended zinc, but this made the condition much worse. Iron made it worse. Virtually all the vitamins made it worse.

FASTING

Since everything made it worse I tried fasting for many days on water only and this made it worse. When fasting makes a condition worse, sometimes the faster will convince themselves that they are going through a "healing crisis" or a "detoxification". I've been through this process enough times so I really understand this thinking.

However in this instance I recalled so many times in the past when I thought I was "toxic" and needed to fast to cleanse, I eventually discovered I was suffering from a nutrient deficiency. So when fasting made my deteriorating health condition, which I later found out was hyperthyroidism, worse, I reasoned that I was suffering from a deficiency of some nutrient which must be very rare and little understood.

FINDING THE RIGHT STARTING POINT

As I was searching the "rare nutrients" in nutrition books and experimenting with these, I eventually discovered that the combination of copper, biotin, and trace elements made me feel better. It didn't take long either, just a few hours after taking copper and the trace elements and only minutes after taking biotin. I was basically copper deficient but for the copper to be utilized properly in my body, it took a combination of some trace element and biotin to be present at the same time.

One of my beliefs is that when you find the right nutrient, the one that is the most deficient, and start supplementing that one, you'll feel benefits within hours and significant improvement within days. Usually the most deficient nutrient in hyperthyroidism is copper and this is the best starting point, but this is not always the case. We will explore the other possibilities also.

Sometimes you may start supplementing the most deficient nutrient, but within days this deficiency will be corrected to the point where another nutrient becomes the most deficient. At this point, you'll get declining benefits or even negative effects from continuing to take that first nutrient and will only keep improving if the next deficient nutrient is added. Then in turn, you will keep having to add additional nutrients in the order of the seriousness of their deficiencies. Also, the inter-dependencies of the nutrients become important. One nutrient may not be utilizable until another nutrient is present.

If all this sounds complicated, it is. Fortunately it is possible by trial and error to get everything corrected and restore health. However, the usual path back to health is frequently three steps forward, two steps back, three steps forward, etc. Satisfying progress is accomplished gradually, but there are very frustrating times when you think you know what should happen, but it doesn't. Always keep in mind that the development of the best program for the nutritional correction of thyroid disease is still in the experimental phase. We are making progress, but still have a long way to go before the perfect program is identified.

GETTING STARTED

If you have hyperthyroidism to the point of serious symptoms such as thyroid storms and periods of uncontrolled rapid heart beat, then the very first step is seeing a doctor and getting a prescription for either Tapazole or Propylthiouracil (PTU) which are antithyroid medications. While there is some concern about their long term safety and some people may have reactions to them, I consider them generally safe and far preferable to having a thyroid storm which can be fatal. Please see the section on thyroid drugs for further information.

With the assumption that your serious symptoms are under control with the use of an antithyroid drug, let's look at correcting the underlying deficiencies that I believe are responsible for creating hyperthyroidism.

MAGNESIUM

First, however, let's look at magnesium and calcium. Magnesium is a mineral that gets deficient in hyperthyroidism, probably as a consequence of the disease rather than as a cause of the disease. Magnesium deficiency has been shown to produce rapid heart rate and arrhythmia (irregular heart rate). Look at the magnesium file for details. Rapid heart rate is the most serious and life-threatening symptom of hyperthyroidism since it can lead to a heart attack and death. As far as I can see the rapid heart rate is primarily the result of a deficiency of magnesium, so magnesium supplementation is a very wise step.

Because magnesium and calcium are one of the pairs of minerals that work together, supplementing one requires supplementing the other. Supplementing magnesium alone will work to an extent, but eventually calcium needs to be added to prevent muscle cramping and bone and tooth deterioration. However, taking calcium without magnesium is one of the worst things you can do in hyperthyroidism, because this increases the magnesium deficiency and increases the heart rate and arrhythmia. This is one of the reasons why dairy products, which are high in calcium and low in magnesium, need to be restricted until magnesium levels are replenished.

Every person with hyperthyroidism should have a bottle of magnesium on hand for emergencies. It can save your life. Studies have shown that magnesium given to heart attack victims (without hyperthyroidism) greatly improves their chances of living and avoiding further heart attacks. Supplementing magnesium on a daily basis and using it for periods of rapid heart rate is very valuable.

Most healthy people can use a calcium/magnesium supplement with two parts of calcium to one part of magnesium (a 2:1 ratio). Others find that a 3:2 ratio works best for them. I've found for myself and others in the group have found that a calcium/magnesium supplement with a 1:1 ratio works best because it provides extra magnesium. Others have found that taking more magnesium than calcium is best for them. Even if you take a 1:1 ratio cal/mag supplement, keep a bottle of magnesium at hand and with you when you travel. It's your best first aid kit if you run into a stressful situation or somehow get your cal/mag ratio disturbed through diet.

While magnesium and calcium are the first supplements for hyperts, I don't believe that deficiencies of these are the cause of hyperthyroidism. Practically all people with thyroid disease show high or unbalanced levels of sodium, potassium, calcium, and magnesium in their hair. I believe that as copper, iron, zinc, and the other deficient nutrients are replenished and get into balance, the need for calcium and magnesium supplementation will gradually subside and these two minerals and sodium and potassium will come back into balance.

OTHER MINERALS

With my present understanding of hyperthyroidism, I believe that the critical deficiencies are primarily minerals and possibly some vitamins.

These are the key minerals which seem to be involved in hyperthyroidism:

Deficient minerals:

- Copper
- Iron
- Sulfur
- Possibly Silver
- Magnesium

Minerals in excess:

- Zinc
- Cadmium
- Aluminum

We want to supplement the minerals that are deficient and stop the intake of the minerals that are in excess.

The key mineral deficiency is usually copper, but remember that there are two cases of this:

- 1. Where copper is really deficient**
- 2. Where copper is being stored, shows high in the hair, and is not being utilized by the body properly.**

COPPER

In the first case, supplementation of copper (about 5 mgs. per day) should be tried as the first step. If this proves beneficial, then it should be continued until the benefits diminish. At that point, a B complex (50 mgs.) with 50 mgs. of extra niacin and 600 mcg. of extra biotin, should be added. Also, iron (about 18 mgs. per day) and sulfur (about 500-1000 mgs. of MSM) should be added.

IRON

Failure to commence iron supplementation once copper starts getting replenished can lead to iron deficiency and iron-deficiency anemia. Since copper was deficient, the body does not have a great store of iron. Once copper is begun, this limited store of iron will be used up rather rapidly. Iron deficiency can be deduced from increasing symptoms of (1) anemia evidenced by dizziness when standing or reduced capacity to exercise and (2) feeling worse after taking copper or vitamin B-2 or eating high copper foods like chocolate, beans, nuts, crab, or lobster.

SULFUR

While iron may be the next major deficiency to correct after commencing copper supplementation, it is usually not the only one. Probably the next mineral to get deficient will be sulfur, evidenced by increasing aches and pains in the joints. Taking MSM should alleviate these symptoms. Since copper, iron, and sulfur work together to form the structural components of the joints, excesses and deficiencies of any one of this trio affects the other two. In arthritis, it appears that copper and sulfur become deficient leaving iron deposits remaining to irritate the joint.

ZINC

Eventually zinc will get deficient and the symptoms of zinc deficiency can seem similar to copper deficiency. Because zinc and copper combine to form one of the body's prime antioxidants, copper,zinc superoxide dismutase (cu,zn-SOD), a deficiency of zinc can lead to a deficiency of this antioxidant. A deficiency of SOD appears to be a part of hyperthyroidism, so a zinc deficiency can sometimes be the reason.

Beyond these key minerals, there can be deficiencies of selenium, silicon, chromium, or possibly tungsten. There is more information on these minerals and various vitamins in the Supplement List and in their individual files under Nutrients and Toxics.

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SUPPLEMENT LIST

Before you read the supplement list (click on the hypertext to the left) read the following guidelines about taking nutritional supplements.

SUPPLEMENTING WITH ESSENTIAL NUTRIENTS

Taking nutritional supplements is an incredible tool that we have at our disposal. However, this is a tool with the proverbial double-edge. While it's possible to reverse a deficiency, correct an imbalance of nutrients, and thereby restore health, it is also possible to unbalance our body's nutrients and create disease.

You will read in many books on nutrition about the need to keep the B complex vitamins balanced. There are four B vitamins usually mentioned that need to be taken in approximately equal amounts: B-1 (thiamine), B-2 (riboflavin), B-3 (niacin or niacinamide), and B-6 (pyridoxine). This is very good advice because taking large amounts of some, but not all, of these can eventually create problems.

What most nutritionists and authors of books on nutrition fail to emphasize is that virtually all nutrients need to be kept in balance and that taking any one nutrient for enough time can create an imbalance which creates health problems.

For example, I always had read that vitamin C is wonderful, protects you from a myriad of diseases including cancer, and the more you take the better off you'll be. Linus Pauling, the Nobel prize winning scientist, wrote a book on vitamin C in which he reported keeping terminal cancer patients alive for long beyond expectation by giving them very large doses of vitamin C, sometimes up to 50 grams or more a day. This is a very large amount considering that the Minimum Daily Requirement is less than 100 milligrams and 1 gram is a large amount.

In 1997 on the basis of this information I was taking 10 grams of vitamin C every day and feeling great just as I expected. However, in the middle of feeling great I developed hyperthyroidism, which as you probably know is a very serious disease. In my subsequent studies I found that taking very large amounts of vitamin C can deplete copper. As you will read elsewhere, I feel that copper deficiency is a key factor that causes hyperthyroidism.

Other nutrients seem to work the same way. For example, taking excess vitamin E seems to aggravate hyperthyroidism because it depletes selenium, the mineral that works with vitamin E. Zinc, which is on every nutritionist's "must take" list, can deplete copper if taken in excess without also supplementing copper. The minerals manganese and chromium work as a pair in various functions and taking either one of them without the other can deplete the one not taken. These minerals are important for thyroid health.

Copper and iron work together to form hemoglobin. If you become deficient in either one, you can get anemic--either iron-deficiency anemia or copper-deficiency anemia. Many people have reported to me that they have been found anemic by their doctors and been given large amounts of iron to correct the problem. Usually the anemia failed to improve. One woman took close to 200 mgs of iron per day for a long time and when her anemia didn't improve, her doctor put her in the hospital for an iron-transfusion, a process in which an extremely large amount of iron is given intravenously. Not only did this not help, but she became extremely ill and was ill for days.

When these people who told me about these experiences had thyroid disease, my first guess was that they were deficient in copper and not iron. When they began supplementing with copper, their anemia improved. I believe that taking the extra iron without copper further depleted their copper and worsened their thyroid health.

It's possible to go on and on through the list of essential nutrients and discovering more and more relationships between nutrients in which taking excess amounts of one can cause deficiencies of others to worsen. I can't think of any nutrient that this principle doesn't apply to.

To get back to the B complex example mentioned first, I believe that vitamins work with and facilitate the utilization of specific minerals. For example, vitamin B-6 is known to be the vitamin that facilitates zinc metabolism. When B-6 is recommended for any condition, such as carpal tunnel syndrome, then it can be assumed that zinc will also benefit the situation if taken with B-6.

It seems that the other B complex vitamins, B-1, B-2, and B-3 facilitate copper metabolism. If this is correct, then you can see that taking excessive amounts of B-6 alone could eventually lead to a copper deficiency. On the other hand, taking B-1, B-2, and B-3 without B-6 could eventually lead to deficiencies of B-6 and zinc. If this were done long enough, then I would expect the person to develop sore wrists, the beginning symptom of carpal tunnel syndrome and itchy skin, another symptom of zinc deficiency.

The message that I want to emphasize is to try to balance your nutrients, not unbalance them. If you are starting with a deficiency, then taking a nutrient such as copper or zinc can gradually correct that deficiency. However, at some point, the opposite mineral needs to be supplemented to prevent that mineral from becoming deficient.

As we attempt to correct deficiencies and nutrient imbalances, we don't want to create other deficiencies and imbalances. We want to move toward balance and then stay there. To achieve this, it's necessary to gradually change the nutrients taken and move toward a more balanced supplementation schedule. For example, when rebalancing copper and zinc, you might start out with a 1:1 ratio of zinc to copper if you were hyper, and a 15:1 ratio if you were hypo. Gradually as you recover you'll want to change that ratio to a ratio that is right for you. For women that might be 5:1 if you were hyper, and 8:1 if you were hypo. For a man, the ratio will probably be higher because of the greater need for zinc.

One way to prevent creating imbalances as you work toward correcting deficiencies is to not take supplements every day. Some people take them every other or every third day. During my recovery I took them about 5 days a week, but this may have been too much. Not only will using this interval method of supplementation work toward preventing imbalances from developing, it will prevent your body from becoming dependent on getting "easy nutrients."

Another good idea is to not take excessive amounts of nutrients. Doubling the intake of a nutrient does not mean that you'll get well twice as fast. There is a limit to your body's ability to take up and incorporate the nutrient. For example, our bodies need about 2.5-3 mgs of copper per day. Taking two to three times that amount or 5-8 mgs per day is reasonable. It is not reasonable to take 15 or more mgs per day. The same is true for zinc. We need about 15 mgs a day so supplementing 50 mgs per day for hypos is reasonable. It's not reasonable to take 100 or more mgs per day.

We can say that nutrients have a physiological range of the quantity and when that normal range is exceeded, the nutrient is being used as a drug. When a nutrient is used in large amounts it has different physiological effects. For example, one mineral might be given in very large amounts to prevent the absorption of its antagonistic mineral. This is not using the mineral for nutritional needs, but using it as a drug to control another function.

When a nutrient is taken in excessive amounts it can have toxic effects. These effects may be the result of causing other nutrient deficiencies. Vitamins and minerals generally have different toxicities in large amounts. Vitamins have a larger range over which they are non-toxic. Sometimes you can take a vitamin in amounts 100 times the recommended amount without toxic effects. Minerals, on the other hand, generally have a low ratio of the toxic amount to the recommended amount. Often this ratio is as low as 6:1. For example, selenium is often taken in amounts of 200-400 mcgs, but taking 1200 mcgs or more a day can prove toxic.

B COMPLEX VITAMINS

There are also different types of vitamins with different toxicity to recommended amount ratios. The B vitamins and most vitamins are water soluble and are readily excreted if taken in excessive amounts. These vitamins can be taken in larger amounts because of this safety feature.

Even though there is relative safety in taking large amounts of B vitamins, I would like to offer this caution. If you look in the Nutrition Almanac you'll see that most of the B vitamins are needed in only small amounts. The impact of taking large amounts of these over a long period of time can be negative.

For example, niacin is recommended to people with heart disease and high blood pressure and a few years ago, people were taking up to 1200-2000 mgs of niacin per day. While niacin is one of the most abundant vitamins in the body, taking this much was found to cause liver damage. Niacin does seem to facilitate copper uptake and it's possible that prolonged use could lead to an excessive buildup of copper in the liver (beyond the amount needed for normal health) which could be damaging. Whether this is the mechanism by which niacin causes liver damage is something I have not been able to find out, but this seems possible.

Because people with thyroid disease may also have livers which are not functioning at 100%, I would recommend not taking excessive amounts of the B vitamins. Niacin in particular should probably not be taken in amounts over 300 mgs per day for an extended period. Taking it with copper to speed up copper uptake for a short duration is probably fine, but just don't make it a long term practice.

Problems stemming from taking the other B vitamins for a long period of time are less documented, but probably also exist. Just be careful and keep your B vitamin intake to a reasonable amount such as 50 mgs of each per day and then take breaks. Use the B vitamins to help rebuild mineral stores which have become deficient, but don't continue taking them beyond what is necessary.

OIL SOLUBLE VITAMINS: A, D, E, K

The oil soluble vitamins, A, D, E, and K, however, accumulate in the body and are stored. These do not need to be taken every day, but if they are taken in excessive amounts over a long period of time can accumulate to dangerous levels. Symptoms of toxic amounts of A and D are headaches. If you take 100,000 units of vitamin A for several months, this toxic level can be easily reached. It's not necessary to take high amounts of these vitamins and often less is better.

Pay attention to the amounts of nutrients recommended in the Supplement Schedule. These are generally safe for most people. However, you may be different and be more sensitive to these nutrients.

While I don't believe that it's possible to be allergic to an essential nutrient, you may experience negative symptoms after taking one. I use these negative reactions to try to determine what is deficient. For example, if you take zinc and feel dreadful afterward, I would suspect that you have a copper deficiency.

Many people are aware that they have sensitivities. Many people with thyroid disorders also have multiple chemical sensitivities or sensitivities to essential nutrients. These sensitivities represent deficiencies of nutrients and as these deficiencies are corrected, the sensitivities will gradually disappear. However, before these deficiencies are corrected, you may experience very negative reactions to taking moderate amounts of nutrients. Use the information on this site to try to determine what deficiencies you have and work on them.

If you know that you have sensitivities, be very careful and don't take any nutrients in the recommended amounts. Cut these amounts down significantly. Be safe, not sorry. The following supplement list will be changed from time to time as new information warrants. I will try to make an announcement in the what's new section if there is a significant change, but check back to this list occasionally. Here is the supplement list:

Supplement List

LIST OF NUTRIENTS FOR HYPERTHYROIDISM AND HYPOTHYROIDISM

(Warning: Use this list with caution and get advice from your physician before using these recommended supplements. The recommended amounts of these nutrients are for experimental purposes only and the potential effects of these nutrients on your health are unknown. You must be responsible for your own health and for knowing the consequences of taking these recommended supplements. I think these are reasonable amounts of these nutrients, but I am not a physician and do not know your health situation. This list is only my best guess about what might help these diseases. What has helped me or another person may cause adverse reactions in you. Consult your own physician.)

GENERAL STRATEGY

I consider hyperthyroidism and hypothyroidism (including Graves' disease and Hashimoto's thyroiditis) as different phases of the same disease. I'm quite confident that both are caused by nutrient deficiencies, but hyperthyroidism is the result when the deficiencies become more severe.

Hypers: Everything that I've experienced myself, seen in others, and read about in scientific studies indicates that the primary deficiencies involved in hyperthyroidism are copper and iron. The balance between copper and zinc seems to be critically important in determining the rate of thyroid hormone production. Copper slows down the thyroid while zinc increases thyroid action. Copper should be supplemented first and if zinc is presently being supplemented it should be discontinued for two to three weeks or until the thyroid slows down. Copper absorption and utilization is increased by molybdenum and the B-complex vitamins, including extra biotin and PABA. Zinc is essential for health but excess amounts may increase thyroid hormone production. You will have to experiment to determine how much zinc you can take. Try to maintain a zinc/copper ratio of about 3:1 to 5:1 at first.

Most hypers and hypos are deficient in iron. Iron may be low because of insufficient intake or deficiencies of minerals such as manganese, copper, or cobalt (vitamin B-12), or B vitamins, which are essential for iron utilization. Copper and iron work together to form hemoglobin and need to be supplemented together. Supplementing with either alone can lead to a deficiency of the other.

Studies show that a deficiency of selenium usually causes a decrease in the conversion of T4 to T3. However under abnormal conditions, a deficiency of selenium can cause the body to increase conversion of T4 to T3 which can lead to higher levels of T3. Selenium is very important for normal thyroid function. Start by taking 100 micrograms per day and gradually increase up to 300 micrograms.

All of the supplements listed are necessary either to correct the underlying causes of hyperthyroidism or to supplement nutrients which are used up by the hyper metabolism.

HYPOS: Many nutrient deficiencies may cause hypothyroidism. The two main nutrients which may be deficient are selenium and zinc. Selenium may become deficient if there are excessive amounts of toxic metals being ingested, such as mercury from silver amalgam dental fillings. The more mercury or other toxic metals ingested, the more selenium you'll need. Start with 200 micrograms of selenium and work up to 400 micrograms. You may need more selenium if you have many amalgam fillings. The B-complex vitamins, especially B-6, facilitate zinc metabolism. Also the amino acid L-cysteine is important in zinc metabolism. Iron, manganese, and chromium are often deficient in hypos. Some hypos may be so deficient in minerals that they are close to becoming hyper. If you are experiencing nighttime rapid heart beat, then you are close and should also supplement with copper.

FOODS

PROTEIN, FAT, AND CARBOHYDRATE

Research studies show that animals fed low protein and/or low fat diets with adequate calories will become hyperthyroid. Low calorie diets with proper ratios of protein and fat tend to make animals hypothyroid. In other words, a diet high in carbohydrates and low in protein and fats will cause an increased production of thyroid hormones and a feeling of higher energy levels. However, the increased energy levels and activity without adequate protein and fat in the diet will cause the body to cannibalize the body's fat and protein stores and may lead to hyperthyroidism.

Studies also seem to show that liver disease such as cirrhosis or hepatitis and pancreatic disease such as pancreatitis interfere with protein and fat digestion and may therefore lead to hyperthyroidism. I am studying this to determine how to restore the health of the liver and pancreas. It appears that a high protein and high fat diet along with digestive enzymes, PABA, and phosphatidylcholine (along with the other recommended supplements) may be the best way to heal the liver and pancreas.

Sam Queen, author of the book, Chronic Mercury Toxicity, told me that autoimmune diseases, such as Grave's disease, are caused by low protein intake or inadequate protein digestion. I am looking for further information on this theory also.

Many foods and supplements which lower blood lipids and which would be recommended for lowering cholesterol (low density lipoproteins or LDLs) seem to have an adverse effect on hypers. It's possible that hypers need to consume more LDLs and avoid all lipid lowering foods such as garlic. This is contrary to most health advice, but hyperthyroidism seems to be a condition where the metabolism is opposite to that found in the majority of people and the opposite approach is needed.

SPECIFIC FOODS THAT MAY HELP

HYPERS: Radish, especially daikon; horseradish; carrots and carrot juice; cruciferous vegetables.

SPECIFIC FOODS AND SUPPLEMENTS WHICH MAY HURT

HYPERS: Any lipid (fat) lowering food or supplement, such as: garlic; ginseng; octacosanol; or other body-building supplements which are commonly used to lose fat.

TOXIC HEAVY METALS

There is a possibility that toxic heavy metals play a causative role in thyroid disease. Several of the group members who have had hair analyses done have high levels of mercury, aluminum, and other metals and also low sodium/potassium (Na/K) ratio. It appears that toxic metals may disrupt the Na/K ratio and thereby interfere with cellular absorption of essential nutrients. This hypothesis is also under investigation.

Sam Queen states that toxic metals are excreted from the body along with bile which is produced in the liver. Sufficient dietary fat is essential for bile production. He states that dairy fat works better than fat found in meat and recommends the consumption of 2-4 ounces of butter a day. I think that 4-6 ounces of high fat cheese such as cheddar would be equivalent.

SUNSHINE

I found that sunshine seemed to help me and other people may have had similar experiences. During my recovery (after I started taking copper), whenever I would spend some time in the sun I would feel better the next day. Recently I've read about a hormone called solatriol which is produced in the skin under the influence of sunshine. One researcher states that it affects many hormone-producing tissues, including the thyroid. We know that the sun helps the skin produce vitamin D, which is really a hormone rather than a vitamin. Solatriol is a second, separate hormone produced by the sun and I intend to research this to see how it is involved in thyroid problems.

We know that copper is used by the body to produce melanin, which is the dark pigment which colors the skin and protects against sun damage. PABA seems to be involved in this metabolism and this is the reason that many sunscreens contain PABA. My present theory is that sunshine on a person who is deficient in copper and/or PABA will result in an increase in those deficiencies and therefore may become more likely to get hyperT. However, sunshine on a person who is getting an adequate amount of copper and PABA may be very beneficial in helping the person recover from hyperT. This is just my theory, but if this is true then we could expect that persons who become more sensitive to the sun and who burn more easily may be copper deficient and therefore likely to develop hyperT.

LIST OF SUPPLEMENTS

Thyroid conditions, especially hyperthyroidism, are characterized by serious nutritional deficiencies. The following list of supplements helped me and others to recover from hyperthyroidism and hypothyroidism and are important to correct the nutritional deficiencies which seem to cause these thyroid conditions. All of these nutrients have been shown to be essential for human life. While hypos may do well by selecting a good multiple vitamin/mineral supplement and adding to it as necessary, hypers have found it necessary to obtain these supplements singly so that the ratios can be changed as needed and so that certain minerals like manganese and iodine can be avoided until the body can once again tolerate these. This list is not intended as a "buffet" from which you can pick and choose. I consider each nutrient listed here important and possibly necessary for improving the thyroid diseases.

MINERALS

BORON

(Increases estrogen which suppresses thyroid function.)

HYPERS: 3-6 mg per day.

HYPOS: Probably don't need extra, unless estrogen is low. Usually hypos have high estrogen and low progesterone and testosterone.

CALCIUM and MAGNESIUM

(Regulates heart rate and builds bone.)

HYPERS: Take with magnesium, 1:1 ratio to suppress "thyroid storms. HyperT interferes with calcium metabolism and promotes osteoporosis, so take at least 1000 mg each of calcium and magnesium.

HYPOS: Take cal/mag in a 2:1 ratio, as needed, perhaps 600/300 mg.

CHROMIUM

(Involved in glucose metabolism and insulin production. The conversion of T4 to T3 is influenced by insulin, which is probably the reason why diabetics have low thyroid function.)

HYPERS: 200 mcg per day.

HYPOS: 400 mcg per day.

COPPER

(Copper seems to be the most important mineral for hypers to take. Copper deficiency has been shown to cause elevated levels of thyroid hormones. It is also essential for monoamine oxidase production which degrades hormones after they have fulfilled their function. Take on full stomach, since it may produce nausea at first.)

HYPERS: 6-10 mg per day. Copper is the most important mineral for hyperT, so take copper first.

HYPOS: 0-3 mg per day. Hypos may have excess copper which is suppressing the thyroid.

IODINE

(Kelp) (Most essential mineral for thyroid hormone production--deficiency of iodine and/or selenium causes goiter, a swelling of the thyroid gland. A goiter is the body's attempt to increase the production of thyroid hormones from an inadequate supply of nutrients. Replenishing those nutrients will enable the body to resorb the goitrous tissue and allow the thyroid to return to its normal size.)

HYPERS: Don't take iodine or kelp until copper is built up. In cases of goiter, supplementing with iodine with insufficient selenium will make the goiter worse. Once copper has been supplemented for awhile, test with one kelp tablet. If hyper symptoms are not

increased, gradually increase the kelp up to 6 tablets per day.

HYPOS: Start with one table per day and build up slowly to 6 tablets per day.

IRON

(Iron is a critical mineral, because while it is very necessary and often low in thyroid disease, iron intake without a corresponding intake of copper can deplete copper. Iron works with copper to build hemoglobin, so therefore too much of either can deplete the other. Usually in hyperthyroidism, copper is deficient and has to be built up first. Once it is replenished, iron supplementation with the copper (probably in a ratio of no more than 5:1, iron:copper) will then help both minerals get built up. If hyper symptoms increase, stop or reduce the iron.) In hypothyroidism, iron is probably more deficient than copper and so should be supplemented first. Once iron is built up then a small amount (2-3 mg) of copper can be added. Iron increases body temperature by increasing norepinephrine and increasing cellular oxygen, which helps the low body temperature problem in hypothyroidism. Iron is known as the strength mineral.)

HYPERS: After copper has been supplemented for a few days, try a small amount of iron. Gradually increase to about 18 mg.

HYPOS: Take 18-36 mg per day.

LITHIUM

(Lithium, sodium, and potassium are important components in the cellular pumps that transport minerals and amino acids across cell membranes. A deficiency of lithium may cause the mineral and amino acid deficiencies we see in hyperthyroidism. Studies have indicated that manic-depression may develop from a lithium deficiency (hyperthyroidism is associated with manic-depression) and some psychiatric patients get hyperthyroidism when lithium treatment is abruptly ended. Limiting sodium and potassium intake for hypers seems important in helping correct the imbalance that may be the result of a lithium deficiency. It also appears that hypos may need more sodium and potassium and perhaps less lithium. As of 7-3-99 I am studying lithium and its relationship to sodium and potassium and hope to be able to add more information to this soon. Lithium is available as a supplement called lithium orotate from www.vitaminshoppe.com in a 120 mg dosage. Most nutrition books including the Nutrition Almanac do not even mention lithium, so I've been unable to find any information on a reasonable amount for supplementation.. Because hyperT is associated with an abrupt termination of lithium supplementation, be careful.)

HYPERS: Lithium orotate 120 mg. My best guess is to take one or two a day. (I am presently trying to determine what the proper dosage. I've taken up to four a day without any immediate noticeable effects.) It may be beneficial to limit sodium and potassium intake until lithium is replenished.

HYPOS: Avoid. Ensure adequate intake of sodium and potassium.

MAGNESIUM

(Essential for thyroid function and appears deficient in both hypos and hypers.)

(See instructions under calcium.)

MANGANESE

(Assists iron metabolism and plays a role in the production of thyroid hormone. The hair analyses of both hypers and hypos show that most are deficient in manganese and chromium. These two minerals work together. Manganese should not be taken by hypers without also taking copper and iron. I believe that manganese and chromium should be taken together and too much of one or the other may disrupt the balance between the two. It's possible that once copper is built up, the body will tolerate more manganese and chromium and these two minerals are probably essential for complete recovery from thyroid disease.)

HYPERS: 5-10 mg per day. Make sure copper and iron are supplemented before manganese is started. If hyper symptoms are experienced, suspect manganese or zinc.

HYPOS: Take 10-20 mg per day.

MOLYBDENUM

(Assists copper utilization. Deficiency symptoms are similar to hyper symptoms.)

HYPERS: Take 250-500 mcg per day.

HYPOS: Unknown

POTASSIUM

(Increases cellular response to T3.)

HYPERS: Unknown

HYPOS: Eat high potassium foods like bananas and potatoes.

SELENIUM

(The essential mineral component of 5'-deiodinase enzymes which convert the prohormone T4 to the cellular active hormone T3. Deficiency of selenium will cause "low T3 Syndrome" where T4 levels are normal but T3 is low. Selenium and/or iodine deficiencies cause goiter. Selenium is the most important mineral to counter the toxic effects of heavy metals. Selenium is essential for production of glutathione peroxidase which is one of the three most important antioxidant defenses of the body. Can be toxic at levels of over 1000 mcg per day. Goiter will result from a selenium deficiency (or iodine deficiency), and many hypers and hypos have goiter.)

HYPERS: Take 200-600 mcg per day. If you have a known high level of mercury or other toxic metal, consider taking more. Start at 100 mcg and work up slowly.

HYPOS: Take 200-600 mcg of selenium per day. Mercury in silver amalgam fillings uses up selenium for detoxification. High amounts of amalgam fillings may require more selenium. Don't take over 600 mcg.

SILICON

(Supplement known as silica, from the plant horsetail. Assists collagen formation and seems to have thyroid function. Helps to

antagonize aluminum which may cause copper excretion and hyperthyroidism.)

HYPERS: Take 2 per day. One information source recommends taking rests from this supplement, like 3 days on, then 2 days off. I've used it every day for about a year with no negative symptoms.

HYPOS: Same as Hypers.

SILVER

(Next to nothing is known about silver and the thyroid, but my guess is that there is some connection. Silver is just below copper in the Periodic Table and therefore has similar chemical properties. Copper and zinc have electrical properties and can be used to make a battery. Silver has similar but better electrical conductivity properties than copper, so there is the possibility that it is important for the same reasons copper is.

However, there is information that leads me to suspect that silver may be very important in controlling TED (thyroid eye disease.) As you will see in the cadmium file and the TED file, I suspect that cadmium (high in tobacco) is one of the prime causes of TED. Cadmium is just to the right of silver in the Periodic Table and probably an excess of cadmium will interfere with silver absorption. Silver has been shown in studies to inhibit fibroblast proliferation and this is the mechanism by which TED develops. See [Silver](#).

I took colloidal silver during my recovery from hyperthyroidism, but have been unable to ascertain if it was important in the healing process or not. I can at least say that it didn't hurt. I did not develop TED. My suggestion is to take 5 drops of colloidal silver per day or follow the directions on the bottle whether you are hyper or hypo.)

HYPERS: 5 Drops of Colloidal silver per day.

HYPOS: Same.

SULFUR

(Supplement known as MSM--methylsulfonylmethane. Works with copper in many functions and may get depleted with copper supplementation. Deficiency causes aches in joints and muscles.)

HYPERS: After copper and iron are built up, start MSM (or when joints get sore.) Common supplement amounts are 1000-3000 mg.

HYPOS: Take 1000-3000 mg.

TRACE ELEMENTS

(Contains small amounts of all minerals. May be important in supplying unknown necessary trace elements. Ionized form best, colloidal form second best. Trace elements can also be obtained from seafoods.)

HYPERS: Supplement with recommended amount unless the iodine,

manganese, or zinc content increase hyper symptoms. If so, take sporadically. If you can't tolerate this at all, take copper and molybdenum until copper is built up and then re-try.

HYPOS: Take recommended amount.

VANADIUM

(I am still researching this, but vanadium seems to be involved in thyroid function. High vanadium levels have been found in the hair of manic/depressives. This means it may be a thyroid stimulant. Available as a supplement, vanadyl sulfate.)

HYPERS: Avoid. I am pretty sure hypers should never take vanadium. Whenever I've used it I've had increased hyper symptoms.

HYPOS: Unknown. There are reports that a vanadium deficiency is a part of diabetes and since many hypothyroids have either diabetes or hypoglycemia, it's possible that hypos are deficient. From my experience I feel vanadium stimulates the thyroid, but I would be very careful with this until more is known.

ZINC

(Works with copper, but also may increase thyroid function. This mechanism is unknown, but zinc may spare selenium because it also detoxifies heavy metals. May increase progesterone production, which stimulates thyroid hormone production. The optimum zinc to copper ratio is about 8:1, but hypers need a lower ratio and hypos a higher ratio. Take on full stomach since it may cause nausea. Take in morning as it may keep you awake if taken at night.)

HYPERS: After copper and iron are built up some, try a small amount of zinc. If tolerated take one to five milligrams of zinc per milligram of copper. If hyper symptoms increase, suspect zinc and reduce amount taken. Premenopausal women may find it better to supplement zinc during the first half of the month and use less or no zinc during the second half.

HYPOS: Take 30-100 mg of zinc to increase thyroid production. If rapid heart beat is felt at night or early morning, decrease zinc.

VITAMINS

A and D

(From fish oil. Usual capsules contain 10,000 IU of A and 400 IU of D. There is some evidence indicating that excessive amounts of vitamin D, possibly only the synthetic form added to foods, may be a problem. A study on rats showed that vitamin A deficiency causes hypothyroidism. Hypos have difficulty converting beta carotene to vitamin A, so supplement with a preformed vitamin A, such as from fish oil.)

HYPERS: Take 1-3 capsule per day. Get adequate amounts of sunshine. Several hypers have reported benefits from carrot juice. Hypers have an increased rate of conversion of beta carotene to vitamin A.

HYPOS: 1-3 capsules per day.

B-COMPLEX

(Vitamins usually included in B-complex will be listed separately. Some people may have to take individual B vitamins, while most may have to supplement extra B vitamins to the B-complex. It appears that the best way to get the B vitamins is to take a B-complex supplement (50 mg) with extra biotin (up to 1000 mcg) and extra PABA (up to 500 mg).

HYPERS: Take one or two 50 mg B-complex per day.

HYPOS: Same as Hypers.

B-1 (Thiamine. Believed essential for copper and sulfur metabolism. Also appears important for correcting eye involvement in Grave's. Many drugs including alcohol and tobacco destroy B-1 and I believe this is the mechanism by which these drugs increase the frequency of Grave's and eye involvement.)

HYPERS: Up to 200 mg or more.

HYPOS: Up to 100 mg or more or taken in B-complex.

B-2 (Riboflavin. Believed essential for copper metabolism. Feelings of eye irritation or the sensation of grit under the eyelids indicates B-2 deficiency.)

HYPERS: 100-200 mg.

HYPOS: 100 mg or taken in B-complex.

B-3 (Niacin. Niacinamide is in most multiples. Niacin is a serotonin precursor, which calms and counters the catecholamine hormones which produce feelings of fear and anxiety. Niacin may be better than niacinamide but causes flushing and requires adaptation. If you've never taken niacin before, be aware that you could get a total body flush which makes you hot and itchy all over. It is not dangerous, but many people have gone to the hospital emergency room convinced that they were in real trouble. To minimize the flush, take on a full stomach and start with 25 mg. at a time, before increasing it.)

HYPERS: Take 100-200 mg a day.

HYPOS: Take 100 mg a day.

B-5 (Pantothenic Acid. May be involved in copper metabolism. Important for adrenal health.)

HYPERS: 100-500 mg.

HYPOS: 100-200 mg.

B-6 (Pyridoxine. Essential for zinc deficiency. Hypos are usually deficient in zinc and B-6. Helps regulate sodium/potassium balance which is disturbed in thyroid diseases and helps prevent water retention in the extremities. Sodium/potassium balance controls the transport of essential nutrients into the cells. If you feel pain in the wrist--carpal tunnel syndrome--take extra B-6 and zinc.)

HYPERS: You may not want to take this at first to prevent excess zinc metabolism and possible hyper symptoms, but later, you'll need to take this to balance your B vitamins.

HYPOS: Take 100-200 mg.

B-12 (Contains cobalt. Facilitates iron metabolism and for treatment of anemia. May deplete iron if taken without iron.)

HYPERS: Probably don't need extra B-12. Amount in B-complex is adequate.

HYPOS: May be deficient. Check levels and supplement if necessary.

BIOFLAVONOIDS, RUTIN, QUERCETIN. Many people with thyroid disease, particularly hyperthyroidism, have bleeding gums, a condition which doesn't respond to the usual vitamin C therapy that most health books recommend. Other nutrients often recommended for bleeding gums include bioflavonoids, rutin, and quercetin. It's quite possible that these facilitate collagen formation and may be very important for copper utilization. If this is true then they may be very important in correcting thyroid conditions and care should be taken to eat a high percentage of raw foods and to supplement these nutrients.

HYPERS: Take amounts as directed on bottle.

HYPOS: Same.

CHOLINE and INOSITOL

(Plays an important role in glutathione production. Choline deficiency affects males and females differently and this indicates that it may play a vital role in thyroid diseases.)

HYPERS: Take 500 mg each of choline and inositol.

HYPOS: Same as hypers.

BIOTIN

(Essential for metabolism of branched chain amino acids and may be involved in copper metabolism.)

HYPERS: Take 500-1000 mcg per day. Amount in B-complex is inadequate.

HYPOS: Same as Hypers.

CO-Q-10

(Found to be low in hypers but normal in hypos, CoQ10 protects the heart from damage which may occur in hyperthyroidism. It's possible, but unknown whether CoQ10 will help hypers.)

HYPERS: Take up to 90 mg per day.

HYPOS: Probably don't need it unless heart problems exist, then same as hypers

FOLIC ACID

(May have thyroid functions. Hypers have been found to have adequate levels, but I haven't found information about hypos yet.)

HYPERS: 400 mcg per day. Don't take more than this.

HYPOS: 400 mcg per day.

PABA

(PABA appears to have very wide-ranging benefits for thyroid diseases and for many diseases associated with thyroid diseases. Seems to be a key vitamin that enables copper to be utilized properly. Reports state that excessive amounts may cause nausea, diarrhea, or skin rash, but I believe these symptoms won't occur if PABA is taken with an adequate amount of copper.)

HYPERS: Take 200-500 mg per day. Take in proportion to the copper you are using.

HYPOS: Take 200 mg a day.

PHOSPHATIDYLCHOLINE

(Important source of choline which comes from lecithin and which is recommended as the best supplement to help correct cirrhosis of the liver and to promote liver health. The liver is a key organ for conversion of T4 to T3 and also for the production of bile to eliminate heavy metals like mercury which interrupt enzyme and endocrine function.)

HYPERS: Take (2) 1200 mg capsules a day

HYPOS: Same as hypers.

C

(Vitamin C is a very important vitamin but our society may be overly concerned with getting enough of it. Many foods are supplemented with vitamin C and many people take large amounts to ward off colds and other perceived health threats. When I got hyperthyroidism, I was taking 10 GRAMS of vitamin C a day. I now realize that this was excessive and have cut the amount way down. I now believe that excessive amounts of vitamin C may be a real problem for people with thyroid disease, especially hypers. Lately I've been seeing that deficiencies of antioxidants may be a cause of thyroid disease. I recently ran across a study which showed that cu,zn-superoxide dismutase (SOD) which is one of the main antioxidants of the body, is decreased by vitamin C. This may occur because vitamin C is also an antioxidant and may be taking up some of the free radical scavenging jobs that SOD normally performs. However, we have seen that hypers experience worse hyper symptoms with larger amounts of vitamin C, and there are studies which indicate that high amounts of vitamin C interfere with copper absorption. These facts lead me to think that high amounts of vitamin C may be a contributory cause of lower levels of SOD and thereby contributing to hyperthyroidism. Also, vitamin C interferes with calcium absorption which is another problem that hypers have. I recommend taking a very low amount of vitamin C, if any, especially for hypers. Whether hypos need more is something I'm going to look into.

HYPERS: Take no more than 500 mg per day. You might want to experiment with taking none or 100-200 mg to see what happens.

HYPOS: Unknown, but limit intake to 1000 mg until more is known.

D

(See vitamin A.)

E

(Assists estrogen production, works with selenium, and has other thyroid functions. If you've never taken E before, start with 100 IU and work up slowly.)

HYPERS: 400 IU per day. Not more.

HYPOS: 400 IU per day.

K

(Works with boron to increase estrogen production. Take yogurt occasionally to assist production. Probably unnecessary to take a supplement since intestinal bacteria can make it.)

AMINO ACIDS

CYSTEINE

(Probably the most important amino acid to supplement for hypos. Key precursor to both glutathione and the deiodinase enzymes which convert T4 to T3. Assists zinc utilization, so it may be more important for hypos than hypers. Currently under study.)

HYPERS: Unknown. Currently studying.

HYPOS: Take 500-1000 mg per day.

TYROSINE

(Precursor to the thyroid hormones and the catecholamines.)

HYPERS: Don't supplement.

HYPOS: Take 500 mg per day.

PHENYLALANINE

(Precursor to tyrosine.)

HYPERS: Don't supplement.

HYPOS: Still researching.

TRYPTOPHAN

(Precursor to niacin and serotonin. Serotonin is the inhibitory (calming) hormone which counters the catecholamines (stimulating hormones which produce anxiety and fear.) High intake reduces the uptake of tyrosine. Studies have shown that hyperthyroidism can be induced in animals by a low tryptophan diet. Eating adequate amounts of protein should ensure that you get adequate amounts of tryptophan. If hyperthyroidism is severe or doesn't respond to anything else, you may want to try tryptophan. Pure L-tryptophan is unavailable except through a doctor's prescription, but health food stores are now carrying a metabolite of tryptophan which may work as well.)

HYPERS: May be beneficial.

HYPOS: Probably not necessary.

BRANCHED CHAIN AMINO ACIDS (BCAAs)

(Leucine, isoleucine, and valine. Compete with tyrosine for absorption, so increasing BCAAs may decrease tyrosine absorption and thereby decrease production of the thyroid and catecholamine hormones.)

HYPERS: Beneficial, especially for exercise, sports, and body building. Does not seem to cause hyper symptoms like other protein supplements.

HYPOS: Unknown.

End of list

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Supplement List

LIST OF NUTRIENTS FOR HYPERTHYROIDISM AND HYPOTHYROIDISM

(Warning: Use this list with caution and get advice from your physician before using these recommended supplements. The recommended amounts of these nutrients are for experimental purposes only and the potential effects of these nutrients on your health are unknown. You must be responsible for your own health and for knowing the consequences of taking these recommended supplements. I think these are reasonable amounts of these nutrients, but I am not a physician and do not know your health situation. This list is only my best guess about what might help these diseases. What has helped me or another person may cause adverse reactions in you. Consult your own physician.)

GENERAL STRATEGY

I consider hyperthyroidism and hypothyroidism (including Graves' disease and Hashimoto's thyroiditis) as different phases of the same disease. I'm quite confident that both are caused by nutrient deficiencies, but hyperthyroidism is the result when the deficiencies become more severe.

Hypers: Everything that I've experienced myself, seen in others, and read about in scientific studies indicates that the primary deficiencies involved in hyperthyroidism are copper and iron. The balance between copper and zinc seems to be critically important in determining the rate of thyroid hormone production. Copper slows down the thyroid while zinc increases thyroid action. Copper should be supplemented first and if zinc is presently being supplemented it should be discontinued for two to three weeks or until the thyroid slows down. Copper absorption and utilization is increased by molybdenum and the B-complex vitamins, including extra biotin and PABA. Zinc is essential for health but excess amounts may increase thyroid hormone production. You will have to experiment to determine how much zinc you can take. Try to maintain a zinc/copper ratio of about 3:1 to 5:1 at first.

Most hypers and hypos are deficient in iron. Iron may be low because of insufficient intake or deficiencies of minerals such as manganese, copper, or cobalt (vitamin B-12), or B vitamins, which are essential for iron utilization. Copper and iron work together to form hemoglobin and need to be supplemented together. Supplementing with either alone can lead to a deficiency of the other.

Studies show that a deficiency of selenium usually causes a decrease in the conversion of T4 to T3. However under abnormal conditions, a deficiency of selenium can cause the body to increase conversion of T4 to T3 which can lead to higher levels of T3. Selenium is very important for normal thyroid function. Start by taking 100 micrograms per day and gradually increase up to 300 micrograms.

All of the supplements listed are necessary either to correct the underlying causes of hyperthyroidism or to supplement nutrients which are used up by the hyper metabolism.

HYPOS: Many nutrient deficiencies may cause hypothyroidism. The two main nutrients which may be deficient are selenium and zinc. Selenium may become deficient if there are excessive amounts of toxic metals being ingested, such as mercury from silver amalgam dental fillings. The more mercury or other toxic metals ingested, the more selenium you'll need. Start with 200 micrograms of selenium and work up to 400 micrograms. You may need more selenium if you have many amalgam fillings. The B-complex vitamins, especially B-6, facilitate zinc metabolism. Also the amino acid L-cysteine is important in zinc metabolism. Iron, manganese, and chromium are often deficient in hypos. Some hypos may be so deficient in minerals that they are close to becoming hyper. If you are experiencing nighttime rapid heart beat, then you are close and should also supplement with copper.

FOODS

PROTEIN, FAT, AND CARBOHYDRATE

Research studies show that animals fed low protein and/or low fat diets with adequate calories will become hyperthyroid. Low calorie diets with proper ratios of protein and fat tend to make animals hypothyroid. In other words, a diet high in carbohydrates and low in protein and fats will cause an increased production of thyroid hormones and a feeling of higher energy levels. However, the increased energy levels and activity without adequate protein and fat in the diet will cause the body to cannibalize the body's fat and protein stores and may lead to hyperthyroidism.

Studies also seem to show that liver disease such as cirrhosis or hepatitis and pancreatic disease such as pancreatitis interfere with protein and fat digestion and may therefore lead to hyperthyroidism. As of Feb. 23, 1999, I am studying this to determine how to restore the health of the liver and pancreas. It appears that a high protein and high fat diet along with digestive enzymes, PABA, and phosphatidylcholine (along with the other recommended supplements) may be the best way to heal the liver and pancreas. I have just begun this part of the investigation, so hopefully I'll know more soon.

Sam Queen, author of the book, Chronic Mercury Toxicity, told me that autoimmune diseases, such as Grave's disease, are caused by low protein intake or inadequate protein digestion. I am looking for further information on this theory also.

Many foods and supplements which lower blood lipids and which would be recommended for lowering cholesterol (low density lipoproteins or LDLs) seem to have an adverse effect on hypers. It's possible that hypers need to consume more LDLs and avoid all lipid lowering foods such as garlic. This is contrary to most health advice, but hyperthyroidism seems to be a condition where the metabolism is opposite to that found in the majority of people and the opposite approach is needed.

SPECIFIC FOODS THAT MAY HELP

HYPERS: Radish, especially daikon; horseradish; carrots and carrot juice; cruciferous vegetables.

SPECIFIC FOODS AND SUPPLEMENTS WHICH MAY HURT

HYPERS: Any lipid (fat) lowering food or supplement, such as: garlic; ginseng; octacosanol; or other body-building supplements which are commonly used to lose fat.

TOXIC HEAVY METALS

There is a possibility that toxic heavy metals play a causative role in thyroid disease. Several of the group members who have had hair analyses done have high levels of mercury, aluminum, and other metals and also low sodium/potassium (Na/K) ratio. It appears that toxic metals may disrupt the Na/K ratio and thereby interfere with cellular absorption of essential nutrients. This hypothesis is also under investigation.

Sam Queen states that toxic metals are excreted from the body along with bile which is produced in the liver. Sufficient dietary fat is essential for bile production. He states that dairy fat works better than fat found in meat and recommends the consumption of 2-4 ounces of butter a day. I think that 4-6 ounces of high fat cheese such as cheddar would be equivalent.

SUNSHINE

I found that sunshine seemed to help me and other people may have had similar experiences. During my recovery (after I started taking copper), whenever I would spend some time in the sun I would feel better the next day. Recently I've read about a hormone called solatriol which is produced in the skin under the influence of sunshine. One researcher states that it affects many hormone-producing tissues, including the thyroid. We know that the sun helps the skin produce vitamin D, which is really a hormone rather than a vitamin. Solatriol is a second, separate hormone produced by the sun and I intend to research this to see how it is involved in thyroid problems.

We know that copper is used by the body to produce melanin, which is the dark pigment which colors the skin and protects against sun damage. PABA seems to be involved in this metabolism and this is the reason that many sunscreens contain PABA. My present theory is that sunshine on a person who is deficient in copper and/or PABA will result in an increase in those deficiencies and therefore may become more likely to get hyperT. However, sunshine on a person who is getting an adequate amount of copper and PABA may be very beneficial in helping the person recover from hyperT. This is just my theory, but if this is true then we could expect that persons who become more sensitive to the sun and who burn more easily may be copper deficient and therefore likely to develop hyperT.

LIST OF SUPPLEMENTS

Thyroid conditions, especially hyperthyroidism, are characterized by serious nutritional deficiencies. The following list of supplements helped me and others to recover from hyperthyroidism and hypothyroidism and are important to correct the nutritional deficiencies which seem to cause these thyroid conditions. All of these nutrients have been shown to be essential for human life. While hypos may do well by selecting a good multiple vitamin/mineral supplement and adding to it as necessary, hypers have found it necessary to obtain these supplements singly so that the ratios can be changed as needed and so that certain minerals like manganese and iodine can be avoided until the body can once again tolerate these. This list is not intended as a "buffet" from which you can pick and choose. I consider each nutrient listed here important and possibly necessary for improving the thyroid diseases.

MINERALS

BORON

(Increases estrogen which suppresses thyroid function.)

HYPERS: 3-6 mg per day.

HYPOS: Probably don't need extra, unless estrogen is low. Usually hypos have high estrogen and low progesterone and testosterone.

CALCIUM and MAGNESIUM

(Regulates heart rate and builds bone.)

HYPERS: Take with magnesium, 1:1 ratio to suppress "thyroid storms. HyperT interferes with calcium metabolism and promotes osteoporosis, so take at least 1000 mg each of calcium and magnesium.

HYPOS: Take cal/mag in a 2:1 ratio, as needed, perhaps 600/300 mg.

CHROMIUM

(Involved in glucose metabolism and insulin production. The conversion of T4 to T3 is influenced by insulin, which is probably the reason why diabetics have low thyroid function.)

HYPERS: 200 mcg per day.

HYPOS: 400 mcg per day.

COPPER

(Copper seems to be the most important mineral for hypers to take. Copper deficiency has been shown to cause elevated levels of thyroid hormones. It is also essential for monoamine oxidase production which degrades hormones after they have fulfilled their function. Take on full stomach, since it may produce nausea at first.)

HYPERS: 6-10 mg per day. Copper is the most important mineral for hyperT, so take copper first.

HYPOS: 0-3 mg per day. Hypos may have excess copper which is suppressing the thyroid.

IODINE

(Kelp) (Most essential mineral for thyroid hormone production--deficiency of iodine and/or selenium causes goiter, a swelling of the thyroid gland. A goiter is the body's attempt to increase the production of thyroid hormones from an inadequate supply of nutrients. Replenishing those nutrients will enable the body to resorb the goitrous tissue and allow the thyroid to return to its normal size.)

HYPERS: Don't take iodine or kelp until copper is built up. In cases of goiter, supplementing with iodine with insufficient selenium will make the goiter worse. Once copper has been supplemented for awhile, test with one kelp tablet. If hyper symptoms are not increased, gradually increase the kelp up to 6 tablets per day.

HYPOS: Start with one table per day and build up slowly to 6 tablets per day.

IRON

(Iron is a critical mineral, because while it is very necessary and often low in thyroid disease, iron intake without a corresponding intake of copper can deplete copper. Iron works with copper to build hemoglobin, so therefore too much of either can deplete the other. Usually in hyperthyroidism, copper is deficient and has to be built up first. Once it is replenished, iron supplementation with the copper (probably in a ratio of no more than 5:1, iron:copper) will then help both minerals get built up. If hyper symptoms increase, stop or reduce the iron.) In hypothyroidism, iron is probably more deficient than copper and so should be supplemented first. Once iron is built up then a small amount (2-3 mg) of copper can be added. Iron increases body temperature by increasing norepinephrine

and increasing cellular oxygen, which helps the low body temperature problem in hypothyroidism. Iron is known as the strength mineral.)

HYPERS: After copper has been supplemented for a few days, try a small amount of iron. Gradually increase to about 18 mg.

HYPOS: Take 18-36 mg per day.

LITHIUM

(Lithium, sodium, and potassium are important components in the cellular pumps that transport minerals and amino acids across cell membranes. A deficiency of lithium may cause the mineral and amino acid deficiencies we see in hyperthyroidism. Studies have indicated that manic-depression may develop from a lithium deficiency (hyperthyroidism is associated with manic-depression) and some psychiatric patients get hyperthyroidism when lithium treatment is abruptly ended. Limiting sodium and potassium intake for hypers seems important in helping correct the imbalance that may be the result of a lithium deficiency. It also appears that hypos may need more sodium and potassium and perhaps less lithium. As of 7-3-99 I am studying lithium and its relationship to sodium and potassium and hope to be able to add more information to this soon. Lithium is available as a supplement called lithium orotate from www.vitaminshoppe.com in a 120 mg dosage. Most nutrition books including the Nutrition Almanac do not even mention lithium, so I've been unable to find any information on a reasonable amount for supplementation.. Because hyperT is associated with an abrupt termination of lithium supplementation, be careful.)

HYPERS: Lithium orotate 120 mg. My best guess is to take one or two a day. (I am presently trying to determine what the proper dosage. I've taken up to four a day without any immediate noticeable effects.) It may be beneficial to limit sodium and potassium intake until lithium is replenished.

HYPOS: Avoid. Ensure adequate intake of sodium and potassium.

MAGNESIUM

(While calcium is involved in muscle contraction, magnesium is necessary for muscle relaxation. With inadequate magnesium, muscles will cramp and the heart muscles will not go through a complete relaxation phase, resulting in incomplete heart cycles and irregular heart rhythm. Essential for thyroid function and appears deficient in both hypos and hypers. Magnesium is the best mineral for quick relief of rapid or irregular heart beat. Seems to need calcium and boron for best absorption and utilization. Toxicity is reported to be very low since the kidneys can eliminate up to 60 grams per day.)

HYPERS: Take as needed to control rapid and irregular heart rate. You may require 1000-2000 mgs per day.

HYPOS: Generally take one half as much magnesium as calcium. However, if taking zinc and other minerals results in rapid or irregular heart beat, take magnesium (and calcium and boron) to relieve these symptoms. 300-400 mgs per day is the recommended amount for healthy persons.

MANGANESE

(Assists iron metabolism and plays a role in the production of thyroid hormone. The hair analyses of both hypers and hypos show that most are deficient in manganese and chromium. These two minerals work together. Manganese is an essential mineral for the formation of thyroid hormone, so hypers are unlikely to be deficient. It's conceivable that a manganese deficiency could cause goiter and hypothyroidism. Manganese should not be taken by hypers without also taking copper and iron. I believe that manganese and chromium should be taken together and too much of one or the other may disrupt the balance between the two. It's possible that once copper is built up, the body will tolerate more manganese and chromium and these two minerals are probably essential for complete recovery from thyroid disease.)

HYPERS: Probably not needed but if hair analysis shows low manganese, try 5-10 mg per day. Make sure copper and iron are supplemented before manganese is started. If hyper symptoms are experienced, suspect manganese or zinc.

HYPOS: Take 10-30 mg per day. Try to take about the same amount of manganese as iron.

MOLYBDENUM

(Sept. 17, 2000. My thinking is changing on molybdenum because of a recent report of a hyper who experienced an increase in heart rate after taking molybdenum. While there is some indication that molybdenum might work with copper, there is other indications that tungsten works more with copper and molybdenum is a tungsten antagonist. Please be aware that this is pure speculation since there is next to no information available on this, but I suspect that molybdenum might be more helpful for hypos than hypers. The reason for this thinking is that copper slows thyroid function and molybdenum can decrease copper (possibly by helping utilization?). There are studies indicating that high molybdenum intake in cattle can cause a copper deficiency. Because of conflicting information, my best suggestion is to experiment with molybdenum to see if it helps. Don't take more than 500 mcg at a time. It's very likely that if you do have a molybdenum deficiency it might get corrected by a very small amount, such as (1) 500 mcg. per day for 2-3 weeks. Please let me know your experiences.

HYPERS: Try 250-500 mcg per day. If molybdenum causes increased heart rate or is not low in hair analysis, don't take it.

HYPOS: Try 250-500 mcg per day to see if it helps.

POTASSIUM

Potassium is critical for proper thyroid and heart function. Hypers and hypos seem to often have low potassium levels. There is a condition called hypokalemic periodic paralysis which affects hypers in which potassium levels get really low and the person's muscles lock up. They can become paralyzed and have heart failure from this. This low potassium condition can be corrected with potassium supplementation. My personal experience is that when you have tremors, shaking, or fast or irregular heart rate (heart skipping beats) and magnesium doesn't correct the problem within a few hours, try taking 400-600 mgs of potassium (or eat bananas and/or potatoes). If potassium is the problem, then the tremors and irregular heart rate should correct within 30-60 minutes. I believe that everyone with a thyroid condition should have a bottle of 99 mg potassium with you at all times for emergency use. Magnesium and sodium can deplete potassium, so be aware of this if you are using supplemental magnesium. While the Nutrition Almanac suggests that we need a minimum of 2000 mgs of potassium a day, I think it's better to try to get 3000-4000 mgs a day.

HYPERS: Often low. Have hair analysis to be sure. Try 400-600 mgs when you have tremors or fast or irregular heart rate. Make sure your diet has adequate potassium by eating bananas, potatoes, or other potassium foods. If you are on a low carbohydrate diet (no bananas, potatoes, etc.) you may need to supplement with 1200 or more mgs of potassium daily. I think it's better to get your potassium from foods though.

HYPOS: Same as hypers.

SELENIUM

(The essential mineral component of 5'-deiodinase enzymes which convert the prohormone T4 to the cellular active hormone T3. Deficiency of selenium will cause "low T3 Syndrome" where T4 levels are normal but T3 is low. Selenium and/or iodine deficiencies cause goiter. Selenium is the most important mineral to counter the toxic effects of heavy metals. Selenium is essential for production of glutathione peroxidase which is one of the three most important antioxidant defenses of the body. Can be toxic at levels of over 1000 mcg per day. Goiter will result from a selenium deficiency (or iodine deficiency), and many hypers and hypos have goiter.)

*Note July 4, 2001: A recent study indicates that selenium in the form of selenomethionine is not absorbed as well as selenium from foods. I have used selenomethionine consistently throughout my recovery and feel that it must work. However, if you suspect that you are not getting enough selenium from your selenomethionine supplement, you may want to try a yeast-based selenium. Some people are concerned, as I was, that excess yeast may not be good, especially if they have candida. I believe that candida will respond to correcting iron-deficiency anemia and that a yeast-based selenium might be worth trying even if you have candida. I have been trying a yeast-based selenium for a few weeks and haven't noticed much difference. However, you may want to experiment with both forms to see which works better for you.

HYPERS: Take 200-600 mcg per day. If you have a known high level of mercury or other toxic metal, consider taking more. Start at 100 mcg and work up slowly.

HYPOS: Take 200-600 mcg of selenium per day. Mercury in silver amalgam fillings uses up selenium for detoxification. High amounts of amalgam fillings may require more selenium. Don't take over 600 mcg. per day unless you have an unusually large amount of amalgam fillings (more than 8).

SILICON

(Supplement known as silica, from the plant horsetail. Assists collagen formation and seems to have thyroid function. Helps to antagonize aluminum which may cause copper excretion and hyperthyroidism.)

HYPERS: Take 2 per day. One information source recommends taking rests from this supplement, like 3 days on, then 2 days off. I've used it every day for about a year with no negative symptoms.

HYPOS: Same as Hypers.

SILVER

(Next to nothing is known about silver and the thyroid, but my guess is that there is some connection. Silver is just below copper in the Periodic Table and therefore has similar chemical properties. Copper and zinc have electrical properties and can be used to make a battery. Silver has similar but better electrical conductivity properties than copper, so there is the possibility that it is important for the same reasons copper is. I took colloidal silver during my recovery from hyperthyroidism, but have been unable to ascertain if it was important in the healing process or not. I can at least say that it didn't hurt. My suggestion is to take 5 drops of colloidal silver per day whether you are hyper or hypo.)

HYPERS: 5 Drops of Colloidal silver per day.

HYPOS: Same.

SULFUR

(Supplement known as MSM--methylsulfanylmethane. Works with copper in many functions and may get depleted with copper supplementation. Deficiency causes aches in joints and muscles.)

HYPERS: After copper and iron are built up, start MSM (or when joints get sore.) Common supplement amounts are 1000-3000 mg.

HYPOS: Take 1000-3000 mg.

TRACE ELEMENTS

(Contains small amounts of all minerals. May be important in supplying unknown necessary trace elements. Ionized form best, colloidal form second best. Trace elements can also be obtained from seafoods.)

HYPERS: Supplement with recommended amount unless the iodine,

manganese, or zinc content increase hyper symptoms. If so, take sporadically. If you can't tolerate this at all, take copper and molybdenum until copper is built up and then re-try.

HYPOS: Take recommended amount.

VANADIUM

(I am still researching this, but vanadium seems to be involved in thyroid function. High vanadium levels have been found in the hair of manic/depressives. This means it may be a thyroid stimulant. Available as a supplement, vanadyl sulfate.)

HYPERS: Avoid. I am pretty sure hypers should never take vanadium. Whenever I've used it I've had increased hyper symptoms.

HYPOS: Unknown. There are reports that a vanadium deficiency is a part of diabetes and since many hypothyroids have either diabetes or hypoglycemia, it's possible that hypos are deficient. From my experience I feel vanadium stimulates the thyroid, but I would be very careful with this until more is known.

ZINC

(Works with copper, but also may increase thyroid function. This mechanism is unknown, but zinc may spare selenium because it also detoxifies heavy metals. May increase progesterone production, which stimulates thyroid hormone production. The optimum zinc to copper ratio is about 8:1, but hypers need a lower ratio and hypos a higher ratio. Take on full stomach since it may cause nausea. Take in morning as it may keep you awake if taken at night.)

HYPERS: After copper and iron are built up some, try a small amount of zinc. If tolerated take one to five milligrams of zinc per milligram of copper. If hyper symptoms increase, suspect zinc and reduce amount taken. Premenopausal women may find it better to supplement zinc during the first half of the month and use less or no zinc during the second half.

HYPOS: Take 30-100 mg of zinc to increase thyroid production. If rapid heart beat is felt at night or early morning, decrease zinc.

VITAMINS

A and D

(From fish oil. Usual capsules contain 10,000 IU of A and 400 IU of D. There is some evidence indicating that excessive amounts of vitamin D, possibly only the synthetic form added to foods, may be a problem. A study on rats showed that vitamin A deficiency causes hypothyroidism. Hypos have difficulty converting beta carotene to vitamin A, so supplement with a preformed vitamin A, such as from fish oil.)

HYPERS: Take 1-3 capsule per day. Get adequate amounts of sunshine. Several hypers have reported benefits from carrot juice. Hypers have an increased rate of conversion of beta carotene to vitamin A.

HYPOS: 1-3 capsules per day.

B-COMPLEX

(Vitamins usually included in B-complex will be listed separately. Some people may have to take individual B vitamins, while most may have to supplement extra B vitamins to the B-complex. It appears that the best way to get the B vitamins is to take a B-complex supplement (50 mg) with extra biotin (up to 1000 mcg) and extra PABA (up to 500 mg).

HYPERS: Take one or two 50 mg B-complex per day.

HYPOS: Same as Hypers.

B-1 (Thiamine. Believed essential for copper and sulfur metabolism. Also appears important for correcting eye involvement in Grave's. Many drugs including alcohol and tobacco destroy B-1 and I believe this is the mechanism by which these drugs increase the frequency of Grave's and eye involvement.)

HYPERS: Up to 200 mg or more.

HYPOS: Up to 100 mg or more or taken in B-complex.

B-2 (Riboflavin. Believed essential for copper metabolism. Feelings of eye irritation or the sensation of grit under the eyelids indicates B-2 deficiency.)

HYPERS: 100-200 mg.

HYPOS: 100 mg or taken in B-complex.

B-3 (Niacin. Niacinamide is in most multiples. Niacin is a serotonin precursor, which calms and counters the catecholamine hormones which produce feelings of fear and anxiety. Niacin may be better than niacinamide but causes flushing and requires adaptation. If you've never taken niacin before, be aware that you could get a total body flush which makes you hot and itchy all over. It is not dangerous, but many people have gone to the hospital emergency room convinced that they were in real trouble. To minimize the flush, take on a full stomach and start with 25 mg. at a time, before increasing it.)

HYPERS: Take 100-200 mg a day.

HYPOS: Take 100 mg a day.

B-5 (Pantothenic Acid. May be involved in copper metabolism. Important for adrenal health.)

HYPERS: 100-500 mg.

HYPOS: 100-200 mg.

B-6 (Pyridoxine. Essential for zinc deficiency. Hypos are usually deficient in zinc and B-6. Helps regulate sodium/potassium balance which is disturbed in thyroid diseases and helps prevent water retention in the extremities. Sodium/potassium balance controls the transport of essential nutrients into the cells. If you feel pain in the wrist--carpal tunnel syndrome--take extra B-6 and zinc.)

HYPERS: You may not want to take this at first to prevent excess zinc metabolism and possible hyper symptoms, but later, you'll need to take this to balance your B vitamins.

HYPOS: Take 100-200 mg.

B-12 (Contains cobalt so your levels can be judged by cobalt levels on your hair analysis. Facilitates iron metabolism and for treatment of anemia. May deplete iron if taken without iron. If iron supplementation causes adverse reactions and copper levels are adequate, suspect a B-12 deficiency. B-12 is destroyed in the stomach by stomach acid, so coated B-12 is needed to get it into the intestines for absorption. The sublingual tablets are not as good.)

HYPERS: Probably don't need extra B-12. Amount in B-complex is adequate.

HYPOS: Very likely deficient. Supplement with 1000-5000 mcg.

BIOFLAVONOIDS, RUTIN, QUERCETIN. Many people with thyroid disease, particularly hyperthyroidism, have bleeding gums, a condition which doesn't respond to the usual vitamin C therapy that most health books recommend. Other nutrients often recommended for bleeding gums include bioflavonoids, rutin, and quercetin. It's quite possible that these facilitate collagen formation and may be very important for copper utilization. If this is true then they may be very important in correcting thyroid conditions and care should be taken to eat a high percentage of raw foods and to supplement these nutrients.

HYPERS: Take amounts as directed on bottle.

HYPOS: Same.

CHOLINE and INOSITOL

(Plays an important role in glutathione production. Choline deficiency affects males and females differently and this indicates that it may play a vital role in thyroid diseases.)

HYPERS: Take 500 mg each of choline and inositol.

HYPOS: Same as hypers.

BIOTIN

(Essential for metabolism of branched chain amino acids and may be involved in copper metabolism.)

HYPERS: Take 500-1000 mcg per day. Amount in B-complex is inadequate.

HYPOS: Same as Hypers.

CO-Q-10

(Found to be low in hypers but normal in hypos, CoQ10 protects the heart from damage which may occur in hyperthyroidism. It's possible, but unknown whether CoQ10 will help hypers.)

HYPERS: Take up to 90 mg per day.

HYPOS: Probably don't need it unless heart problems exist, then same as hypers

FOLIC ACID

(May have thyroid functions. Hypers have been found to have adequate levels, but I haven't found information about hypos yet.)

HYPERS: 400 mcg per day. Don't take more than this.

HYPOS: 400 mcg per day.

LUTEIN

(May be important for thyroid health, but is most likely essential for normal eye health. Since most people with hyperthyroidism have eye problems like dry and itchy eyes, lutein is probably very important. Lutein may be extremely important for those with thyroid eye disease (TED).

HYPERS: 2-3 capsules per day.

HYPOS: unknown, experiment to see if it helps.

PABA

(PABA appears to have very wide-ranging benefits for thyroid diseases and for many diseases associated with thyroid diseases. Seems to be a key vitamin that enables copper to be utilized properly. Reports state that excessive amounts may cause nausea, diarrhea, or skin rash, but I believe these symptoms won't occur if PABA is taken with an adequate amount of copper.)

HYPERS: Take 200-500 mg per day. Take in proportion to the copper you are using.

HYPOS: Take 200 mg a day.

PHOSPHATIDYLCHOLINE

(Important source of choline which comes from lecithin and which is recommended as the best supplement to help correct cirrhosis of the liver and to promote liver health. The liver is a key organ for conversion of T4 to T3 and also for the production of bile to eliminate heavy metals like mercury which interrupt enzyme and endocrine function.)

HYPERS: Take (2) 1200 mg capsules a day

HYPOS: Same as hypers.

Vitamin C

(Vitamin C is a very important vitamin but our society may be overly concerned with getting enough of it. Many foods are supplemented with vitamin C and many people take large amounts to ward off colds and other perceived health threats. When I got hyperthyroidism, I was taking 10 GRAMS of vitamin C a day. I now realize that this was excessive and have cut the amount way down. I now believe that excessive amounts of vitamin C may be a real problem for people with thyroid disease, especially hypers. Lately I've been seeing that deficiencies of antioxidants may be a cause of thyroid disease. I recently ran across a study which showed that cu,zn-superoxide dismutase (SOD) which is one of the main antioxidants of the body, is decreased by vitamin C. This may occur because vitamin C is also an antioxidant and may be taking up some of the free radical scavenging jobs that SOD normally performs. However, we have seen that hypers experience worse hyper symptoms with larger amounts of vitamin C, and there are studies which indicate that high amounts of vitamin C interfere with copper absorption. These facts lead me to think that high amounts of vitamin C may be a contributory cause of lower levels of SOD and thereby contributing to hyperthyroidism. Also, vitamin C interferes with calcium absorption which is another problem that hypers have. I recommend taking a very low amount of vitamin C, if any, especially for hypers. Whether hypos need more is something I'm going to look into.

HYPERS: Take no more than 500 mg per day. You might want to experiment with taking none or 100-200 mg to see what happens.

HYPOS: Unknown, but limit intake to 1000 mg until more is known.

Vitamin D

(See vitamin A.)

Vitamin E

(Assists estrogen production, works with selenium, and has other thyroid functions. Because vitamin E assists selenium metabolism, it is quite likely that excess amounts will deplete selenium. I recommend that you don't take more than 100 IU per day. Since vitamin E accumulates in the body, it doesn't matter if you take 100 IU per day for four days or 400 IU once every four days.)

HYPERS: 100 IU per day. Not more.

HYPOS: 100 IU per day.

Vitamin K

(Works with boron to increase estrogen production. Take yogurt occasionally to assist production. Probably unnecessary to take a supplement since intestinal bacteria can make it.)

ANTIOXIDANTS

ALPHA LIPOIC ACID

(A powerful antioxidant which is a lipid and water soluble thiol which has been shown to protect the body from cadmium toxicity.)

HYPERS: 100-300 mgs. per day

HYPOS: Same

AMINO ACIDS

CYSTEINE

(Probably the most important amino acid to supplement for hypos. Key precursor to both glutathione and the deiodinase enzymes which convert T4 to T3. Assists zinc utilization, so it may be more important for hypos than hypers. Currently under study.)

HYPERS: Unknown. Currently studying.

HYPOS: Take 500-1000 mg per day.

TYROSINE

(Precursor to the thyroid hormones and the catecholamines.)

HYPERS: Don't supplement.

HYPOS: Take 500 mg per day.

PHENYLALANINE

(Precursor to tyrosine.)

HYPERS: Don't supplement.

HYPOS: Still researching.

TRYPTOPHAN

(Precursor to niacin and serotonin. Serotonin is the inhibitory (calming) hormone which counters the catecholamines (stimulating hormones which produce anxiety and fear.) High intake reduces the uptake of tyrosine. Studies have shown that hyperthyroidism can be induced in animals by a low tryptophan diet. Eating adequate amounts of protein should ensure that you get adequate amounts of tryptophan. If hyperthyroidism is severe or doesn't respond to anything else, you may want to try tryptophan. Pure L-tryptophan is unavailable except through a doctor's prescription, but health food stores are now carrying a metabolite of tryptophan which may work as well.)

HYPERS: May be beneficial.

HYPOS: Probably not necessary.

BRANCHED CHAIN AMINO ACIDS (BCAAs)

(Leucine, isoleucine, and valine. Compete with tyrosine for absorption, so increasing BCAAs may decrease tyrosine absorption and thereby decrease production of the thyroid and catecholamine hormones.)

HYPERS: Beneficial, especially for exercise, sports, and body building. Does not seem to cause hyper symptoms like other protein supplements.

HYPOS: Unknown.

End of list

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ALUMINUM

Aluminum appears to be a copper antagonist as is cadmium. In the hair analyses that I've seen from people with hyperthyroidism, usually either cadmium or aluminum levels are high. This supports the hypothesis that there are multiple ways that copper can become depleted and lead to hyperthyroidism.

Aluminum is an essential nutrients, but in our society there seems to be a much greater chance of getting too much aluminum rather than too little. Here are some common sources of aluminum that you need to avoid if your hair test shows high aluminum: antiperspirants and underarm deodorants, aluminum cookware (especially dangerous if acid foods like tomatoes are cooked), beverages from aluminum cans, municipal drinking water which often has aluminum compounds added, baking powders, bleached flour, processed cheese, some table salts, some antacids, and breathing in dust when sanding with aluminum oxide sandpaper.

Aluminum file (authors and titles will be added):

"The effect of repeated intraperitoneal administration of deferoxamine, citric, *malic* and succinic acids on the distribution and excretion of aluminum was determined in male Swiss mice which had previously received aluminum nitrate intraperitoneally at a daily dose of 0.27 mmol/kg for five weeks. Chelating agents were administered for two weeks at doses approximately equal to one-fourth of their respective LD50. Treatment with DFOA, citric, *malic* or succinic acids significantly increased the fecal and urinary excretion of aluminum and reduced the concentration of aluminum found in various organs and tissues, with citric acid being the most effective. In sight of these results, citric, *malic* or succinic acids may be considered as alternatives to deferoxamine in aluminum toxicity. However, further investigations are required previous to the possible use of these compounds in human aluminum poisoning." [malic acid for aluminum toxicity.doc](#)

"All the dietary constituents significantly increased the aluminum levels in bone, whereas brain aluminum concentrations were also raised by the intake of lactic, gluconic, *malic*, citric, and oxalic acids. The levels of aluminum found in spleen were significantly increased by gluconic and ascorbic acids, whereas gluconic and oxalic acids also raised the concentrations of aluminum found in kidneys. Because of the wide presence and consumption of the above dietary constituents, in order to prevent aluminum accumulation and toxicity we suggest a drastic limitation of human exposure to aluminum." [malic acid increases brain levels of aluminum.doc](#)

"Aluminum induces impairment of bone formation by the inhibition of osteoblastic function. *Magnesium* enhances bone turnover by through the stimulation of osteoclastic function. Zinc regulates secretion of calcitonin from thyroid gland and influences on bone turnover. Gallium suppresses bone turnover in humoral hypercalcemia of malignancy in a similar mechanism as aluminum and cadmium. Copper induces low bone turnover by both suppressions of osteoblastic and osteoclastic functions. Iodine as the hormonal forms of thyroxine and triiodothyronine enhances bone turnover." [aluminum interferes with bone formation.doc](#)

"High dietary aluminum seemed most toxic when dietary *magnesium* was low enough to cause a marked growth depression (100 micrograms/g). High dietary aluminum elevated the spleen weight/body weight and liver weight/body weight ratios in *magnesium*-deficient, but not in *magnesium*-adequate rats. High dietary aluminum depressed the concentrations of magnesium in bone more markedly in *magnesium*-deficient than adequate rats. On the other hand, aluminum seemed most toxic when dietary boron was not low. Aluminum more markedly depressed growth in boron-supplemented than boron-deprived rats. In the boron-deprived rats fed 400 micrograms *magnesium*/g of diet, high dietary aluminum (1,000 micrograms/g) apparently was beneficial, in experiments 2 and 3, hematocrit, and hemoglobin were actually normalized by high dietary aluminum. Plasma *magnesium* was significantly depressed by high dietary aluminum when the manganese supplement was 50 micrograms/g diet but not when it was 20 micrograms/g diet. On the other hand, growth was more markedly depressed by high dietary aluminum in boron-supplemented rats when the manganese supplement was 20 rather than 50 micrograms/g diet. The findings indicate that the response of rats to high dietary aluminum is influenced by *magnesium*, boron, and manganese nutriture." [aluminum toxicity affected by Mg,B,Mn.doc](#)

Title Severe copper deficiency due to excessive use of an antacid combined with pyloric stenosis.

Author van Kalmthout PM; Engels LG; Bakker HH; Burghouts JT

Source Dig Dis Sci, 27(9):859-61 1982 Sep **Language** Eng **Unique Identifier** 82261179

Literature regarding the biochemistry of aluminum and eight similar ions is reviewed. Close and hitherto unknown similarities were found. A hypothetical model is presented for the metabolism, based on documented direct observations of Al³⁺ and analogies from other ions. Main characteristics are low intestinal absorption, rapid urinary excretion, and slow tissue uptake, mostly in skeleton and reticuloendothelial cells. Intracellular Al³⁺ is probably first confined in the lysosomes but then slowly accumulates in the cell nucleus and chromatin. Large, long-lived cells, e.g., neurons, may be the most liable to this accumulation. In heterochromatin, Al³⁺ levels can be found comparable to those used in leather tanning. It is proposed that an accumulation may take place at a subcellular level without any significant increase in the corresponding tissue concentration. The possible effects of this accumulation are discussed. As Al³⁺ is neurotoxic, the brain metabolism is most interesting. The normal and the lethally toxic brain levels of Al³⁺ are well documented and differ only by a factor of 3-10. The normal brain uptake of Al³⁺ is estimated from data on intestinal uptake of Al³⁺ and brain uptake of radionuclides of similar ions administered intravenously. The uptake is very slow, 1 mg in 36 years, and is consistent with an assumption that Al³⁺ taken up by the brain cannot be eliminated and is therefore accumulated. The possibility that Al³⁺ may cause or contribute to some specific diseases, most of them related to aging, is discussed with the proposed metabolic picture in mind. [aluminum--metabolism and possible health effects.doc](#)

Studies were conducted in order to assess the level of aluminium (Al) in samples of Indian tea, coffee, toothpaste, paan masala (mouth freshener) and baking powder. Leaching of Al from cookware while preparing tea and coffee was also studied. Experiments were also conducted to study the sequential leaching of Al from cookware by preparing tea and coffee in the presence of standard size Al sheets (coupons). A small amount of Al was found to have leached from coupons during preparation of tea. Tea leaves, were found to be a rich source of Al and a maximum of 2.2% Al is extracted in tea infusions. Coffee powder on the other hand was not found to be a rich source of Al. Baking powder was found to be a rich source of Al and 1 kg of cake prepared with 1-3 teaspoon of baking powder may contain 2-12.7 mg of Al in each serving (25 g). Toothpaste also contains a significant quantity of Al, more so, when packed in Al tubes. Ingestion pattern of Al from these items by humans is also discussed. [aluminum in tea.doc](#)

Nutrition Almanac, pg. 100: "Aluminum is easily absorbed by the body and is accumulated in the arteries. Highest concentrations are found in the lungs, liver, thyroid, and brain." "Average amounts in the diet do not interfere with the absorption or utilization of calcium, phosphorus,

zinc, copper, selenium, iron, or magnesium. Fluoride may be interfered with, but more tests must be made."

Carl C. Pfeiffer, Ph.D., M.D.

UNSUSPECTED COPPER AND/OR ALUMINUM POISONING IN PATIENTS AND THE TREATMENT

Many patients have a low blood histamine (histapenia) & high serum copper level. Low histamine patients are typically overstimulated with thoughts racing through their minds making normal ideation difficult. Low histamine children are hyperactive while often healthy in other respects. Serum Cu levels in these patients are abnormally high. The normal level of serum Cu is about 100 mcg%. Since Cu is a brain stimulant and destroys histamine, the elevated serum (and presumably brain Cu) level probably accounts for many symptoms, including the low blood histamine level. The treatment Rx consists of the administration of zinc, manganese, vit. C, niacin, vit. B-12, and folic acid. Folic acid in conjunction with B-12 injections raises blood histamine while lowering the degree of symptomatology. Zn allows for the normal storage of histamine in both the blood cells and the brain. Zn and manganese increase the urinary excretion of copper. Patients with loss of memory frequently have high blood AL levels above 20 ppb. As magnesium, zn and vit C. are given the high blood AL level decreases to normal (less than 10 ppb) and memory improves. Accumulation of AL occurs in various human tissues including blood, brain, liver & bone. Several independent research reports now indicate that a high AL intake may have an adverse effect on memory in the adult (Alzheimer's D.), & may be a factor in learning disabilities & behavioral problems in younger people. Humans do not need AL for any purpose. Individuals with elevated blood AL levels, memory loss & those frequently exposed to AL compounds will find it beneficial to minimize or eliminate all AL sources.

From the bulletin board, February 27, 2002:

Copper anemia from ALUMINIUM

From: Mike

T1: MichaelVmc@AOL.com

Remote User:

Comments

Hello fellow freedom fighters. God bless us with wisdom and freedom from sickness. I thought I should warn anyone who uses Aluminum Oxide sand paper for woodworking, etc. I have always been very careful not to use any aluminum housewares, toothpaste, anti-perspirants, packaged food products, food additives (Watch for baking powder in baked goods). The one fiery dart that the enemy got me with was sand paper. Aluminum Oxide is just one kind of many types of sand paper on the market. All types of sand paper should be used with dust masks, air filters and protective clothing. (Change and wash your clothing before you take off the dust mask).

Johns article on Aluminum is great. Check it out.

John; I do have questions on how to get rid of Aluminum once it is in the system.

Should I stop taking boron? Increase Magnesium, Zinc, Vit.C, Copper?

Here are some of I-I-2001 test results. All symptoms are now gone.

Thanks John for your compassion to help others.

Most symptoms were gone within a few weeks of using the Hyper supplement recommendation.

My hair test showed very high Aluminum, very Low Copper, very low Selenium, Very high Iron, very high Calcium and Magnesium, low Cobalt, low Molybdenum, low Lithium, low Boron, high potassium / normal sodium. All other minerals and toxins were normal.

Thyroid tests= normal according to Doctor. Are they? reference range TSH = 3.2 0.40 - 5.00 t4 = 10.0 5.0 - 12.0 thyroglobulin Auto AB = <0.3 <1.0 Thyroid peroxidase auto AB = 0.5 <2.0 free T-3 = 2.7 2.3 - 4.2 free T-4 = 1.2 0.8 - 1.6

symptoms =fatigue, high heart rate, tremors, anxiety, Joint pain. high blood pressure (135-100).

The doctor said there is nothing wrong with you, except you are under stress.

I think I was Aluminum toxic, which used up my copper, selenium reserve.

Maybe John can explain this better.

Hi Mike,

That is really great information about the use of aluminum oxide sandpaper. I just added it to the aluminum file and you'll see it next time I publish. I don't believe that any nutrition book has mentioned that source, and I, as a woodworker, never thought of it either. It's funny, we work so hard avoiding the trace amounts of some toxic only to expose ourselves to a major source without awareness. I'm glad you discovered that. It might help a lot of people.

I sell wood supplies and abrasives to the wood working industry. I was always surprised by the number of cabinet makers who get hernias. Perhaps this is the answer. The aluminum in the sandpaper decreases their copper.

Since aluminum is a light element, I believe that it's pretty easy to get it back down to normal levels. One thing that I recently noticed is that magnesium (element 12) is right next to aluminum (element 13) in the Periodic Table of Elements. I missed this for years because the Periodic Table is distorted (like the Mercator Map of the world, the Periodic Table would be better represented in three dimensions rather than two).

The elements right next to aluminum are magnesium (to the left), boron (above), silicon (right), and gallium (below). Each of these should be good antagonists for aluminum. I would suggest taking adequate amounts of these. Silicon is found as silica or horsetail extract. Gallium isn't available yet as a supplement, although I acquired some and experimented with it. Indium is right below gallium (and therefore two rows below aluminum) and, interestingly, just to the right of cadmium. This position suggests that indium might be a key element in reducing both cadmium and aluminum. But, alas, indium is not available as a supplement either. Both gallium and indium, however, are available as trace elements in a good trace element supplement.

The relationship of copper to aluminum is interesting, because they do not appear to be right next to each other in the Periodic Table. However, if you use a little freedom with the Table, you could easily see that aluminum and magnesium could be positioned just above copper in the table. Since there are close relationships between magnesium and copper and aluminum and copper, perhaps we need to think of these three minerals as all right next to each other.

The balance between aluminum, magnesium, and copper is a very critical balance that affects thyroid health. Excess aluminum is often seen in the hair of hypers and when copper is replenished, aluminum levels invariably go back down. So the key to getting aluminum back into balance is probably copper along with magnesium. Aluminum toxicity has to be considered a primary way that copper gets depleted, and hence a primary cause of the copper deficiency diseases: collagen failure, hernias, high cholesterol, heart disease, aneurysms, and hyperthyroidism.

So it's possible that aluminum was the beginning of your problems. Once the high aluminum depleted copper, this created other imbalances, like the high iron. High iron, in turn, causes low cobalt, etc.

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ANEMIA

ANEMIA--TYPES AND CAUSES

Many disease conditions are associated with thyroid diseases, but of all these diseases, the one with the highest association is anemia. I read one study which indicated that about one half of all hyperthyroids had clinically diagnosed anemia. It's possible, and to me quite likely, that the other half were also anemic but not diagnosed because they had copper-deficiency anemia and not iron-deficiency anemia.

Anemia is usually caused by a deficiency of hemoglobin which is the oxygen carrying molecule in the red blood cell. While many minerals are important in the body's manufacture of hemoglobin, iron and copper are the most important. A deficiency of either iron or copper will result in anemia, either iron-deficiency anemia or copper-deficiency anemia.

Anemia is often medically diagnosed by determining blood levels of iron and the iron-carrying protein ferritin. This test will determine anemia if the anemia is due to iron deficiency. However, this test will not show if the person has copper-deficiency anemia.

It seems that many doctors are unaware of copper-deficiency anemia and will try to correct all cases of anemia by prescribing very large doses of iron. Since the majority of cases of anemia are probably the result of iron deficiency, then this procedure usually works. However, in copper-deficiency anemia, taking excess amounts of iron will further deplete copper and cause the anemia to worsen. This exact scenario has happened to more than one person in our group.

SYMPTOMS OF ANEMIA

The symptoms of anemia are: rapid heart beat, dizziness upon standing, reduced capacity to exercise, reduced endurance, elevated heart rate when exercising and failure of the heart to return to a normal rate in a reasonable time upon exercise cessation, low physical energy, low mental energy ("brain fog"), feeling of unease which is alleviated by a period of breathing deeply, inability to fall asleep or to sleep well (insomnia), waking up gasping for breath, and an increase of all these symptoms when traveling to a higher altitude (vacationing in the mountains).

All of these symptoms are related to a reduced amount of oxygen getting to the cells. The most serious of these symptoms is the increase in heart rate. Because each red blood cell carries less oxygen to the cells, the heart rate increases to increase the blood flow so that the cells will not be oxygen starved.

CONNECTION BETWEEN ANEMIA AND THYROID DISEASE

Keep in mind that there is no clear-cut proof of this, but I believe that the mineral deficiencies which lead to hypothyroidism and hyperthyroidism bear remarkable similarity to the mineral deficiencies which lead to the two main types of anemia.

Iron-deficiency anemia and hypothyroidism are similar in that in both iron is more deficient than copper. Copper-deficiency anemia and hyperthyroidism are similar in that in both copper is more deficient than iron.

It is an easy step to postulate that anemia is the single most important pre-existing and causative condition in the etiology of hypothyroidism and hyperthyroidism. Hypothyroidism may be the result of iron-deficiency anemia and hyperthyroidism may be the result of copper-deficiency anemia.

Since iron is needed by the body in amounts approximately five times that of copper, then iron deficiency probably occurs more often than copper deficiency. I've read that one-fifth of the world's population suffers from iron deficiency. This may be one of the reasons that hypothyroidism is more common than hyperthyroidism.

WHO GETS ANEMIA AND THYROID DISEASE

Women in their child-bearing years need more iron and copper than women at other ages and men at any age because of the monthly blood loss during menstruation. Pregnancy, child-birth, and nursing place additional mineral drains on this group of women. This age group of women is the same group that is 8-10 times more likely to get thyroid diseases and autoimmune diseases.

When a otherwise healthy teenage girl gets hyperthyroidism right after beginning her period, then it has to be the result of a deficiency of minerals that are depleted by the blood loss. What other explanation could there be? When a woman develops hyperthyroidism during pregnancy or breast feeding, it also indicates a deficiency.

Who else gets anemic and gets thyroid disease? People who exercise excessively like Olympic athletes and they often get anemia and hyperthyroidism. Older men and women, especially if they don't eat much red meat (iron) or drink much beer (copper). Also, people with poor digestion such as those with celiac disease.

WHAT ARE THE MAJOR DEFICIENCIES INVOLVED IN ANEMIA?

Following is a study from the US Dept of Agriculture, which seems to be doing some of the best nutritional research in the country. The study clearly states that copper deficiency causes anemia and serious cardiovascular disease.

Biofactors 1999;10(4):359-75

Cardiovascular effects of dietary copper deficiency.

Saari JT, Schuschke DA

US Department of Agriculture, Agricultural Research Service, Grand Forks Human Nutrition Research Center, ND 58202-9034, USA.
jsaari@gfhnrc.ars.usda.gov

Dietary copper deficiency may impair cardiovascular health by contributing to high blood pressure, enhancement of inflammation, anemia, reduced blood clotting and arteriosclerosis. The purpose of this review is to compile information on the numerous changes of the heart, blood and blood vessels that may contribute to these cardiovascular defects. These alterations include weakened structural integrity of the heart and blood vessels, impairment of the use of energy by the heart, reduced ability of the heart to contract, altered ability of blood vessels to control their diameter and to grow, and altered structure and function of circulating blood cells. The fundamental causes of these changes rest largely on reduced effectiveness of enzymes that depend on copper for their activity.

Zinc is essential for normal iron metabolism and prevention of anemia, but high levels of zinc can depress iron and lead to anemia.

J Am Coll Nutr 1998 Jun;17(3):291-5

Zinc status relates to hematological deficits in middle-aged women.

Nishiyama S, Irida K, Matsubasa T, Higashi A, Matsuda I

Department of Pediatrics, Kumamoto University, School of Medicine, Japan.

OBJECTIVE: The objective of our study was to investigate zinc (Zn) status and the effects of Zn supplementation in relation to iron deficiency anemia in middle-aged women. It is important to define the role of Zn in hematologic abnormalities and to determine the frequency of Zn deficiency. **METHODS:** Fifty-two Japanese women, selected from a health examination survey on 6200 women, had hemoglobin concentrations below 12.0 g/dl, total iron binding capacity (TIBC) below 390 micrograms/dl and fairly normocytomia. These 52 were divided into three groups and we then compared the hematological status before and after iron (group A) or Zn (group B) or iron plus Zn (group C) supplementation. **RESULTS:** After treatment, concentrations of hemoglobin (Hb) increased slightly in groups A and B, but not statistically significant. In group C, Hb levels were significantly increased from 10.8 +/- 1.1 to 12.8 +/- 1.1 g/dl. Furthermore, numbers of RBC and reticulocytes, and concentrations of albumin were also increased significantly. Increased values over 1.0 g/dl of hemoglobin levels were noted in four women (26.6%) in group A, three women (14.2%) in group B and 13 women (81.2%) in group C. **CONCLUSION:** Zn status to some extent can account for hematological abnormalities in middle-aged women. At least 5.0% of middle-aged Japanese women may have Zn deficiency. Normocytic anemia with low TIBC levels may serve as a good indicator of a marginal Zn deficiency.

This study of a hyena which ingested high-zinc coins shows that excessive zinc can cause anemia

J Zoo Wildl Med 1999 Sep;30(3):431-4

Zinc toxicosis in a captive striped hyena (*Hyaena hyaena*).

Agnew DW, Barbiers RB, Poppenga RH, Watson GL

Detroit Zoological Institute, Royal Oak, Michigan 48068, USA.

An 11-yr-old captive-born female striped hyena (*Hyaena hyaena*) acutely developed lameness and swelling of the left front foot with anorexia, depression, and lethargy. **Hematologic evaluation revealed regenerative anemia**, azotemia, and other mild serum electrolyte and mineral abnormalities. Twenty radiographically visible coins and 10 coin fragments were removed by laparotomy and gastrotomy following unsuccessful medical therapy. The animal died during anesthetic recovery. Zinc serum levels were 41.0 ppm at first presentation and 36.0 ppm at the time of surgery, compared with concentrations of 1.78 ppm and 2.82 ppm for serum taken from this female and a male hyena 3 mo previously. Zinc toxicosis was diagnosed based on the similarity of clinical signs to those described in dogs, presence in the stomach of pennies minted after 1982 (when the zinc content of U.S. pennies was increased substantially), necropsy findings, and elevated serum and liver zinc values. The case highlights the risk posed by penny ingestion for subsequent zinc toxicosis in captive omnivores.

WHAT OTHER FACTORS MAY CAUSE ANEMIA?

We have seen that certain minerals like cadmium, aluminum, and mercury are involved in thyroid disease because they deplete copper, iron, zinc, and selenium. Are they also involved in anemia?

Smokers get hyperthyroidism at a higher rate than nonsmokers and the reason is probably the high levels of cadmium in tobacco which depletes copper. Do smokers have a higher rate of anemia than nonsmokers? There are not a lot of studies which directly address this issue, but some that look at it indirectly. The following study suggests that this hypothesis may be true:

Epidemiology 2000 May;11(3):285-91

Smoking and myelodysplastic syndromes.

Bjork J, Albin M, Mauritzson N, Stromberg U, Johansson B, Hagmar L

Department of Occupational and Environmental Medicine, Lund University Hospital, Sweden.

[Medline record in process]

The purpose of this case-control study was to investigate tobacco smoking as a risk factor for myelodysplastic syndromes, emphasizing karyotypic aberrations as markers for exposure and risk differentiation with respect to morphology. We obtained smoking history by interview of 330 cytogenetically investigated adult myelodysplastic syndrome cases and 337 controls, matched with respect to sex, year of birth, and county of living. Smoking for at least 1 year at some time 20 years or less before diagnosis was associated with an elevated relative risk (RR) for primary myelodysplastic syndromes (odds ratio (OR) 1.8; 95% confidence interval (CI) = 1.2-2.7). The results indicated a relation with intensity and duration of smoking as well as a decrease in risk a few years after cessation of smoking. Smoking was associated with an increased RR for primary myelodysplastic syndromes with chromosome 7 abnormalities (OR 5.0; 95% CI = 1.1-23). **Elevated RRs were also seen for refractory anemia (OR 2.5; 95% CI = 1.2-5.6) and for refractory anemia with ringed sideroblasts (OR 3.2; 95% CI = 0.88-12).** The findings suggest that smoking is a risk factor for myelodysplastic syndromes.

PMID: 10784245, UI: 20244831

Following is a very good review which states that cadmium and lead toxicity causes anemia. Extremely interesting is the comment that "

Quoting the study, "Hg++ accumulation in the brains of suckling rats is approx. 10 times higher than in grown animals. Milk increases the bioavailability of Hg++." Does this "10 times" strike a bell for you as it does for me? This is the factor by which women (high in estrogen) are more likely to get hyperthyroidism than men. The evidence is clearly pointing to heavy metal toxicity from cadmium and mercury which is accelerated by estrogen as the causative factor for hyperthyroidism and hypothyroidism.

Z Ernährungswiss 1990 Mar;29(1):54-73

[The toxicological estimation of the heavy metal content (Cd, Hg, Pb) in food for infants and small children].

[Article in German]

Schumann K

Walther-Straub-Institut für Pharmakologie und Toxikologie der Ludwig-Maximilians-Universität, München, FRG.

There are differences between young and adult organisms regarding toxicokinetic aspects and clinical manifestations of heavy metal intoxications. **Chronically, toxic Cd intake causes a microcytotic hypochromic anemia in young rats at lower exposure levels and after shorter exposure periods than in adult animals. Cd absorption is increased by co-administration of milk and in conjunction with iron deficiency.** After long exposure periods toxic Cd concentrations accumulate in the kidney cortex; this process starts very early in life. In 3-year-old children Cd concentrations in the kidney can reach up to one-third of those found in adults. **Hg++ and methyl-Hg can cause Hg encephalopathy, and frequently cause mental retardation in adults. Correspondingly, Hg++ accumulation in the brains of suckling rats is approx. 10 times higher than in grown animals. Milk increases the bioavailability of Hg++.** In suckling rats Hg is bound to a greater extent to ligands in the erythrocytes. Methyl-Hg concentrations in breast milk reach 5% of those in maternal plasma and that is a severe hazard for breastfed children of exposed mothers. Toxic Pb concentrations can lead to Pb encephalopathy. A high percentage of surviving children have seizures and show signs of mental retardation. **Anemia and reduced intelligence scores were recently observed in children after exposure to very low levels of Pb.** Pb absorption is increased in children and after co-administration of milk. There are no definite proofs for carcinogenesis or mutagenesis after oral exposure to Cd, Hg, and Pb in man. Heavy metal concentrations were found in the same order of magnitude in commercial infant formulas and in breast milk. When infant formulas are reconstituted with contaminated tap water, however, Pb and Cd concentrations can be much higher. The average heavy metal uptake from such diets exceeds the provisional tolerable weekly intake levels set by the WHO for adults, calculated on the basis of an average food intake and a downscaled body weight. These considerations do not even provide for differences in absorption and distribution or for the increased sensitivity of children to heavy metal exposure. However, dilution effects for essential heavy metals were observed in fast-growing young children; this effect might be extrapolated to toxic metals. These theoretical considerations are compared with epidemiological evidence. A health statistic from Baltimore shows a decline of Pb intoxications in infants. This observation correlates with a simultaneous decline in exposure to Pb which was due, for example, to decreased use of lead dyes in house paints and the abolition of tin cans for infant food.

What about aluminum? Does high aluminum intake cause anemia? The following study shows that aluminum can interfere with iron absorption and metabolism and contribute to anemia.

Toxicology 2000 Jan 3;142(2):97-109

Effect of dietary aluminum on tissue nonheme iron and ferritin levels in the chick.

Han J, Han J, Dunn MA

Department of Food Science and Human Nutrition, University of Hawaii, Honolulu 96822, USA.

Aluminum toxicity is well documented but the mechanism of action is poorly understood. **In renal failure patients with aluminum overload, disturbances in iron metabolism leading to anemia are apparent.** Few animal models, however, have been used to study the effects of dietary aluminum on iron metabolism. The purpose of this study was to determine if dietary aluminum exposure alters tissue iron and ferritin concentrations in the chick, as has been found in cultured human cells exposed to aluminum. Groups of day-old chicks were fed purified diets containing one of two levels of iron (control or high iron), and one of three levels of aluminum chloride in a 2 x 3 factorial design. Diets were consumed ad libitum for 1 week, then pair-feeding was initiated for 2 more weeks. A seventh group consumed a low iron diet ad libitum for comparative purposes. After the 3-week feeding period, samples of kidney, liver, and intestinal

mucosa were analyzed for nonheme iron and ferritin concentrations by a colorimetric assay and SDS-PAGE, respectively. Results showed that dietary aluminum intake reduced iron stores in liver and intestine, but had no effect on nonheme iron levels in the kidney. Ferritin levels were reduced by aluminum intake in all tissues studied. The decreases in tissue ferritin levels were proportionately more than the decreases in tissue nonheme iron levels. This resulted in increased nonheme iron to ferritin ratios that amounted to as much as 140 and 525% in kidney and intestine, respectively. **These findings are consistent with the interpretation that, in the growing chick, dietary aluminum can inhibit iron absorption, disrupt the regulation of tissue ferritin levels by iron, and potentially alter the compartmentalization and protective sequestration of iron within cells.**

PMID: 10685509, UI: 20147936

The following study shows that aluminum inhibits iron metabolism, red blood cell production (

Acta Physiol Pharmacol Bulg 1998;23(1):27-31

Influence of aluminium on erythropoiesis, iron metabolism and some functional characteristics of erythrocytes in rats.

Ganchev T, Dyankov E, Zacharieva R, Pachalieva I, Velikova M, Kavaldjieva B

Medical Univesity of Varna, Department of Physiology, Bulgaria.

The increased aluminium (Al) levels in serum of patients with chronic renal failure on hemodialysis are associated with impaired erythropoiesis and iron metabolism. The long term Al loading of rats (20 to 90 days) has similar effect. Data are still lacking about the effects after short-term aluminium treatment. The 7 day's treatment with $Al_2(SO_4)_3$ in a dose 67.5 mg/kg b. w., i. m. significantly decreased hemoglobin, hematocrit, incorporation of ^{59}Fe in newly formed erythrocytes and increased reticulocytes in absolute and relative counts. We observed a mild degree hypochromic, ferropenic, microcytic anemia and polychromazia in the available macrocytes. The immature erythroblasts were predominant forms in the erythroblastogram while the number of mature erythroblasts was decreased. Index of maturation of erythroblasts was lower, indicating inhibited erythroblast maturation. Plasma iron, TIBC, transferrin saturation and ^{59}Fe absorption in the experimental group were significantly decreased. Spontaneous and mechanical hemolysis of erythrocytes were lower while erythrocyte deformability was increased. **Obviously, Al treatment inhibits erythropoiesis and iron metabolism, probably hinders hemoglobin synthesis and erythroid cell maturation but does not affect the studied functional characteristics of mature erythrocytes negatively.**

PMID: 10347617, UI: 99276965

What about mercury from dental amalgam fillings? Can mercury cause anemia? The following study indicates that it does.

: Sci Total Environ 1990 Dec 1;99(1-2):23-35

The relationship between mercury from dental amalgam and the cardiovascular system.

Siblerud RL

Department of Physiology, College of Veterinary Medicine and Biological Sciences, Colorado State University, Fort Collins 80523.

The findings presented here suggest that mercury poisoning from dental amalgam may play a role in the etiology of cardiovascular disorders. Comparisons between subjects with and without amalgam showed amalgam-bearing subjects had significantly higher blood pressure, lower heart rate, lower hemoglobin, and lower hematocrit. **Hemoglobin, hematocrit, and red blood cells were significantly lower when correlated to increased levels of urine mercury. The amalgam subjects had a greater incidence of chest pains, tachycardia, anemia, fatigue, tiring easily, and being tired in the morning.** The data suggest that inorganic mercury poisoning from dental amalgam does affect the cardiovascular system.

PMID: 2270468, UI: 91102526

Here's another study indicating that mercury intoxication causes anemia where the patient used Mercurochrome as a topical antiseptic. No one uses Mercurochrome anymore, do they? Anyone know if this product is still sold? If you have this or any other mercury compound in your medicine chest, get rid of it now.

Acta Med Scand 1979;205(6):463-6

A case of merbromin (Mercurochrome) intoxication possibly resulting in aplastic anemia.

Slee PH, den Ottolander GJ, de Wolff FA

A patient is described who appeared to be suffering from mercury intoxication caused by local application of merbromin to an operation wound and who developed aplastic anemia, which we ascribed to merbromin.

PMID: 88168, UI: 79206133

As the following study states, a great many factors can affect the blood and lead to anemia.

Folia Med Cracov 1993;34(1-4):29-47

Immunotoxic and hematotoxic effects of occupational exposures.

Lisiewicz J

Department of Hematology, Collegium Medicum, Jagiellonian University, Krakow.

The toxic effects of environmental factors at work places on the hematopoietic and immune systems are of basic importance due to the time of exposure, lasting on average 8 hours daily during one week. Porphyrinurias and porphyrias have been observed after exposure to hexachlorobenzene, chlorinated dibenzodioxins, polychlorinated biphenyls, polybrominated biphenyls, vinyl chloride and lead.

Aplastic anemia may occur after exposure to benzene, pesticides, arsenic, cadmium and copper compounds. Megaloblastic anemia has been noted in subjects exposed to arsenic, chlordane, benzene and nitrous oxide. Methemoglobinemia is induced by aromatic nitro and amino compounds. Hemolytic reactions caused by arsenic, methyl chloride, naphthalene, lead, cadmium and mercury compounds represent a separate problem. Immunodeficiencies resulting in decreased antitumor and antiinfectious immunity have been reported in subjects exposed to asbestos, ozone, dimethylsulphoxide, vinylidene chloride, and benzene homologues. Lymphocytopenia may be induced by manganese, lead, toluene and industrial noise. Neutropenia was marked after exposure to carbon disulphide, arsenic compounds, benzene and electromagnetic fields. Only a few reports concern the lymphocyte T3, T4 and T8 subpopulations. Electromagnetic fields (microwaves) cause an imbalance of that subpopulation, consisting of a decrease in the T8 cell count. The neutrophil enzymes, such as myeloperoxidase and alkaline phosphatase, decrease in their activity after exposure to polychlorinated biphenyls, carbon disulphide, chlorobenzene and DDT. A majority of agents cited include genotoxic effects reflected in chromosome aberrations and increased sister chromatid exchange and abnormal unscheduled DNA synthesis. Leukemia or lymphoma risk is increased after exposure to pesticides, electromagnetic fields, benzene and irradiation.

ANEMIA AND HYPERTHYROIDISM

What studies show that anemia is associated with hyperthyroidism? In the following study, 38 out of 100 hyperthyroid patients were found to be have hypochromic anemia (low hemoglobin). Also the 38 anemic patients had significantly higher levels of thyroid hormones than the 62 without anemia. Additionally, the authors state that iron deficiency, B-12 deficiency, and folic acid deficiency could all be excluded as possible causes of the anemia. This makes sense to me. The conclusion, as I see it: copper-deficiency anemia. Since copper gets used up in de-activating thyroid hormones, treating the hyperthyroidism normalized the anemia because the excessive drain on copper reserves produced by high thyroid hormones was ended.

Z Gesamte Inn Med 1981 Mar 15;36(6):203-8

[Hyperthyroidism and anemia].

[Article in German]

Hambsch K, Fischer H, Langpeter D, Muller P

In a random test of 100 patients with hyperthyroidism with clinical and paraclinical ascertainment of the diagnosis in **38 cases normo-hypochromic, normocytary anaemias of different expression were found. In the patients with anaemia the serum hormone values were statistically significantly higher than in the 62 patients without anaemia.** Also cardiotoxic and hepatotoxic findings were more frequently to be proved in patients with anaemia. **A causal iron deficiency, deficit of vitamin B12 or folic acid as well as a haemolytic component of the induction of anaemia could vastly be excluded.** By means of the treatment of the basic disease and metabolic balance a normalisation of hemoglobin was achieved without additional medication. From the results of the examinations is concluded that above all a thyreotoxic damage is responsible for the development of the anaemia. In cases of oligo-symptomatic hyperthyroidism part from hepatotoxicity and cardiotoxicity also anaemias may become a leading symptom.

ANEMIA AND HYPOTHYROIDISM

The following study states that 20-60% of patients with hypothyroidism are anemic. It also states that "Anemia is often the first sign of hypothyroidism." Very important is the observation that anemia in hypothyroidism is often not diagnosed because hypothyroids have a lower volume of plasma which causes a false high estimation of the amount of hemoglobin in the blood.

Med Pregl 1999 Mar-May;52(3-5):136-40

[Anemia in hypothyroidism].

[Article in Serbo-Croatian (Roman)]

Antonijevic N, Nesovic M, Trbojevic B, Milosevic R

Poliklinika Vizim, Beograd.

INTRODUCTION: **Anemias are diagnosed in 20-60% patients with hypothyroidism.** Real values of the degree of anemia are estimated by radioisotopic analysis due to the **lower volume of plasma in hypothyroidism causing false high levels of hemoglobin in blood. Anemia is often the first sign of hypothyroidism.** Diagnosis of hypothyroidism should be considered in every case of anemia with uncertain etiology because sometimes signs of overt hypothyroidism needn't necessarily be evident. Microcytic, macrocytic and normocytic are regularly described anemias. CLASSIFICATION: Microcytic anemia is usually ascribed to malabsorption of iron and loss of iron by menorrhagia. Macrocytic anemia is caused by malabsorption of vitamin B12, folic acid, pernicious anemia and inadequate nutrition. **Pernicious anemia occurs 20 times more frequently in patients with hypothyroidism than generally.** Macrocytosis is found in up to 55% patients with hypothyroidism and may result from the insufficiency of the thyroid hormones themselves without nutritive deficit. Normocytic anemia, so-called uncomplicated anemia, arises due to thyroid hormones deficit itself not followed by nutritive deficit. This type of anemia is considered to be an adaptation to a decreased basal metabolism. Thyroid hormones directly or indirectly, through erythropoietin, stimulate growth of erythroid colonies (BFU-E, CFU-E). Normocytic anemia is characterized by reticulopenia, hypoplasia of erythroid lineage, decreased level of erythropoietin, mainly regular erythrocyte survival. Acanthocytosis findings in cytologic blood smear suggest hypothyroidism in about 90% of cases.

The following study shows that anemia is also present in congenital hypothyroidism (in infants born with hypothyroidism) just as it is found in adult hypothyroids. Note that the authors of this study, as most researchers in the field, try to attribute the anemia to the effect of low thyroid hormones, despite the fact that the anemia persists even after thyroid hormone supplementation. It seems that no one is seeing that the same mineral deficiencies which cause anemia (iron and zinc), cause hypothyroidism.

J Endocrinol Invest 1996 Oct;19(9):613-9

Anemia in infants with congenital hypothyroidism diagnosed by neonatal screening.

Franzese A, Salerno M, Argenziano A, Buongiovanni C, Limauro R, Tenore A

Dipartimento di Pediatria, Università di Napoli, Italy.

Although anemia is a common finding in adult hypothyroid patients, there are no studies on anemia in hypothyroid infants. The aim of this study, therefore, was to review the hematologic status during the first year of life in 50 infants with congenital hypothyroidism detected through the regional neonatal screening program. The mean age at diagnosis was 23.7 +/- 6.5 days and treatment was initially begun with a mean L-thyroxine dose of 6.8 +/- 1.3 micrograms/kg/day. Clinical and haematological assessments were performed at diagnosis, 3, 6 and 12 months of age. The patients were divided in 2 groups based on whether T4 serum concentration at diagnosis was < 3 micrograms/dl (Group A) or > or = 3 micrograms/dl (Group B). Data for hemoglobin (Hb), hematocrit (Ht), red cells count (RCC), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), serum iron and ferritin were expressed as Standard Deviation Score (SDS). Although at diagnosis the mean value of Hb-SDS, Ht-SDS and RCC-SDS were in the low-normal range in both groups, at 3 months of age the values in Group A (Hb -1.9 +/- 0.79; Ht -2.34 +/- 1.02; RCC -1.56 +/- 1.25) were significantly lower than in Group B (Hb -1.14 +/- 0.78, p < 0.005; Ht -1.59 +/- 0.94, p < 0.05; RCC -0.55 +/- 1.32, p < 0.02). A rise of the Hb, Ht and RCC values was observed in both groups from 6 to 12 months. The mean values of MCV-SDS and MCH-SDS were in the normal range at diagnosis in both groups, decrease progressively at 3 and 6 months and returned to normal at 12 months of age; no differences were found between the 2 groups at any time. Mean Hb levels at 3 months of age were correlated with mean serum T4 at diagnosis (r = 0.30, p < 0.05). **The present results indicate that anemia is a frequent finding in infants with congenital hypothyroidism** and is dependent on the degree of neonatal hypothyroidism and imply that hypothyroidism during development may produce persisting changes even after thyroid replacement has begun.

Iron deficiency may be a factor in anemia, hypothyroidism, and myxedema (pretibial myxedema is a swelling of the front of the shin from fibroblast proliferation, a condition associated with thyroid disease and thyroid eye disease). There are not many studies which have looked at iron levels in myxedema, but the following study is suggestive.

Lik Sprava 1999 Jun;(4):148-50

[Iron-deficiency anemia as a hematological mask of myxedema].

[Article in Ukrainian]

Vydyborets' SV

An atypical course of myxedema manifested by iron-deficiency anemia is described that proved to be a diagnostic challenge. Pathogenetic mechanisms of origination are analyzed.

There are numerous studies to suggest that both hypothyroidism and hyperthyroidism are diseases which stem from the same deficiencies which cause anemia.

Other studies indicate that the same metals which we have seen contribute to thyroid disease also contribute to anemia. It appears that toxicities from metals like cadmium, mercury, lead, and aluminum are involved in the etiologies of both diseases.

An understanding of anemia can be very important for the person suffering from thyroid disease. The symptoms of anemia listed above should be watched for so that you can more closely monitor the effects of your supplement and eating programs on your thyroid disease. By eating to correct anemia, you should be able to correct your thyroid disease.

ADDENDUM--THALASSEMIA

Thalassemia is an inherited form of anemia and there are two main types: alpha-thalassemia in which there is a decreased rate of synthesis of the alpha chains of hemoglobin; and beta-thalassemia in which there is a decreased rate of synthesis of the beta chains of hemoglobin.

Cardiac arrhythmia (irregular heart rate) is a symptom of thalassemia induced anemia as it is of anemia caused by nutrient deficiencies. Amiodarone is a potassium channel blocking drug which is used to control the cardiac arrhythmia caused by thalassemia.

Amiodarone is known to induce hypothyroidism and hyperthyroidism. Following is a study about thyroid dysfunction induced by Amiodarone treatment.

J Endocrinol Invest 1999 Jan;22(1):55-63

High prevalence of thyroid dysfunction in adult patients with beta-thalassemia major submitted to amiodarone treatment.

Mariotti S, Loviselli A, Murenu S, Sau F, Valentino L, Mandas A, Vacquer S, Martino E, Balestrieri A, Lai ME

Dipartimento di Scienze Mediche M. Aresu, Università di Cagliari, Italy.

Amiodarone may induce hyper- or hypothyroidism. Patients with beta-Thalassemia Major (beta-Thal) have an increased prevalence of

primary hypothyroidism and often require amiodarone for hemosiderotic cardiomyopathy. Aim of this study was to retrospectively evaluate thyroid function in beta-Thal adult patients on long-term amiodarone. The study group consisted of twenty-two (21 males, 1 female; age: 23-36 yr) beta-Thal patients submitted to long-term (3-48 months) amiodarone therapy from January 1991 to July 1996. Controls included 73 beta-Thal patients (23 males and 50 females aged 25-35 yr) not treated with amiodarone. In all cases serum free thyroid hormones, thyrotropin and thyroid autoantibodies were evaluated. A higher prevalence of overt hypothyroidism (5/22 [22.7%]) as compared to controls (3/73 [4.1%], $p=0.02$) was found in beta-Thal patients ≤ 3 months after starting amiodarone, while the prevalence of subclinical hypothyroidism was similar in amiodarone-treated (18.2%) and untreated (15%) beta-Thal patients. Overt hypothyroidism resolved spontaneously after amiodarone withdrawal in 1 case, while the remaining patients were maintained euthyroid on amiodarone by L-thyroxine administration. After 21-47 months of amiodarone therapy, 3 patients (13.6%) developed thyrotoxicosis (2 overt and 1 subclinical), which remitted shortly after amiodarone withdrawal. No case of hyperthyroidism was observed in beta-Thal controls ($p=0.012$ vs amiodarone-treated patients). In conclusion, amiodarone administration is often associated in adult beta-Thal patients to a rapid progression of the pre-existing subclinical hypothyroidism, but transient thyrotoxicosis may also be observed after a longer period of therapy. These findings should be carefully considered in the management of these patients.

The following study shows that anemia and iron deficiency cause tongue pain. Thus tongue abnormalities may be a useful indicator of anemia.

Am J Med Sci 1999 Nov;318(5):324-9

The pathophysiology of glossal pain in patients with iron deficiency and anemia.

Osaki T, Ueta E, Arisawa K, Kitamura Y, Matsugi N

Department of Oral Surgery, Kochi Medical School, Nankoku-city, Japan.

BACKGROUND: It is well known that prolonged anemia causes atrophy of tongue papillae, glossal pain, and dysphagia, but it is uncertain whether iron (Fe) deficiency induces glossal pain without any objective manifestation. To resolve this matter, the relationship between Fe deficiency and glossal pain was examined. **METHODS:** Eighteen patients with Fe deficiency and 7 anemic patients manifesting spontaneous irritation or pain of the tongue without any objective abnormalities participated in this study. To ascertain the cause of glossal pain and the oral pathophysiology in Fe deficiency and anemia, peripheral blood was examined and the glossal pain threshold and salivary flow rates (SFRs) were estimated along with *Candida albicans* cell culture tests. **RESULTS:** Compared with patients with Fe deficiency, those with anemia had a longer history of tongue pain. In patients with anemia, painful areas of the tongue were more numerous than in patients with Fe deficiency. Pain thresholds were decreased in the painful portions, and both nonstimulated and stimulated SFRs were suppressed. Each patient was treated with oral Fe; within 2 months, most patients exhibited increased serum ferritin level ($P < 0.02$, paired t-test), pain threshold ($P < 0.05$) and salivation ($P < 0.05$) and glossal pain subsided. **CONCLUSIONS:** Fe deficiency causes glossal pain and the degree of glossal pain increases as Fe deficiency advances to anemia, manifesting hyposalivation and abnormalities of glossal papillae.

Protein Discovery Leads Researchers to New Suspect in Iron Anemia

From: <http://www.berkeley.edu/news/berkeleyan/1999/0224/protein.html>

By Kathy Scalise, Public Affairs
Posted February 24, 1999

If you're slugging down iron pills but remain weak and anemic, the culprit may not be iron at all, but another metal: copper. A new genetic find explaining why is described by a Berkeley scientist and his colleagues in this month's issue of the journal *Nature Genetics*.

The researchers discovered a protein, hephaestin, that appears critical for moving iron to the bloodstream. This protein contains copper and cannot be produced in the absence of copper. Thus in some cases, having too little copper present even with an ample iron supply might cause anemia, said the lead author on the paper, Assistant Professor Christopher Vulpe of the Division of Nutrition and Toxicology in the College of Natural Resources.

The new protein may also help explain what Vulpe describes as the number one inherited disease in Caucasians, hemochromatosis. It results from too much iron in the body and can cause diabetes if it kills insulin-producing cells in the pancreas, or "iron heart" if too much of the metal accumulates in that organ and causes cardiac arrest.

Vulpe's collaborators on the project included researchers from UC San Francisco, the University of Utah and the University of Queensland in Australia.

Hephaestin was isolated from mice and named after the Greek god for metal-working, Hephaestus. The protein is produced by the gene *Heph*, also discovered by the researchers and reported in the *Nature* paper, and is tethered to the membrane of intestinal cells. The researchers suspect it is a "multi-copper ferroxidase" protein that contains copper and works on iron molecules.

Vulpe led the original study while a postdoctoral fellow in the laboratory of Professor Jane Gitschier of

UCSF. Gitschier said in a recent UCSF statement that "more work needs to be done to determine if and how often genetic defects in iron transport occur in humans."

In describing the possible role of the new protein, Vulpe traced the path of iron through the body.

Iron, he said, usually originates in the food supply, either as "heme," a cage of iron that transports oxygen in blood and comes mainly from meats, or as "free" iron from other sources. Both kinds of iron are processed by the gut -- stomach and intestine -- where they are converted by means not well understood to a form of iron readily used by the body. Finally, the iron winds up in the intestinal epithelial cells, ready for export to red blood cells, muscle tissue and organs.

But somehow "it has to get out of the gut and into the bloodstream," said Vulpe.

This is particularly difficult, he said, because the so-called "hydrophobic" intestinal membrane wants to reject the charged iron molecule.

So hephaestin comes into play. Probably acting as a helper molecule forming a complex with a yet unknown transport protein, it allows iron to make its way through the membrane.

In fact, hephaestin may act like an "on/off" switch to control the flow of iron into the body, said Vulpe. Perhaps in the presence of hephaestin, more iron is pumped into the blood, and when hephaestin stops production, the pumping also soon halts.

While a certain amount of iron is vital for survival, about 10 percent of infants and women of childbearing age in the U.S. -- about 8.5 million people -- are iron deficient. Many other people suffer from having too much iron circulating in the body, a syndrome called hemochromatosis, which can also have toxic effects.

When the body functions correctly, excess iron remains trapped in the intestine and is harmlessly excreted. Disease results only after too much iron escapes from the intestine and into the blood.

The UC researchers plan to investigate whether hephaestin plays a role in hemochromatosis.

They suspect improper regulation of the Heph gene may result

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Thyroiditis, Schmyroiditis.....

From: Christine
T1: tnccline@prodigy.net
Remote User:

Comments

Hello Lisianthus -

If this endo/specialist is "hard to talk to" then he's NOT really much of a doctor, is he? If there is no communication between the patient and the doctor, how in the world are you going to get well??

Stick with the PCP, or find another PCP who knows about thyroid disorders. You don't need an endo who lies to you about the testing, keeps guessing about the treatment, and regards you as someone who can easily be jacked around.

From the beginning, it sounds like they've been trying to put you into a squeeze play over this RAIU. Continue to refuse it! Most of what the docs need to know can be done with bloodwork. They DO get mad when you refuse their cheap, toxic, diagnostic testing.

If you haven't already done so, please read the info from John and Elaine on RAIU, accessible from the homepage of this website.

What's going on with this lab test runaround is the old soft-soap routine. "Oh, yeah honey, we'll run those tests. No problem." Then you get the minimum from the lab, which sadly enough can sometimes be just a TSH. They will run only what they have to and nothing else.

If they based their decision about treatment on just the TSH, they need to go back to school.

First off, you need to ask that they let you see the lab order. Then you can SEE, and make remarks about, what they have ordered.

Even that isn't foolproof, though. I've seen labs refuse to run a blood test as simple as a "total" T-4, because "they never run THAT test" and was given no reason other than that. The doc had marked both "free" and "total" T-4 on the lab request.....

If they refuse to let you see the order, say this:

"Just because I don't have 8 years plus of medical school under my belt, does that make me an ignorant moron? I want to participate in my health because I know my body better than anyone else on earth. If you can't bring yourself to lend me enough credibility and respect to keep me informed, then please direct me to a REAL doctor who will."

OK, you need:

T-4 (both "free" and "total" if you can get them)

Note re T-4 - I've had the "free" T-4 in the "normal" range and the "total" be above normal, so getting both of these can give you more info when you are having symptoms.

T-3 ("total" or "free")

Note re T-3 - In many cases a high T-3 level can be causing hyper symptoms, while the T-4 tests are within normal limits.

TSH

Note re TSH - It can remain very low (0.01, 0.03, etc.) for an extended period of time, even if your thyroid levels get so low that you suffer hypO symptoms. If you've been hyper for a while, the TSH can remain low (indicating hyper) for months on end.

THE TSH BY ITSELF IS A USELESS MEASURE OF THYROID FUNCTION.

And just guess how many doctors will put the HYPO patient on anti-thyroid drugs such as Tapazole and PTU, based solely on this woefully inadequate TSH testing. Sometimes it's ignorance on the doctor's part, and sometimes it's because that's ALL THE LAB WILL RUN.

It's possible to have the THYROID levels below normal, leaving you extremely hypo and reduced to a zombie with zero energy, and still have a "non-existent" TSH.

**ANTIBODY TESTING*

To determine whether your thyroiditis is autoimmune or not. This CAN affect the treatment options.

ANTI-THYROGLOBULIN and ANTI-PEROXIDASE.

Obviously they're just going to keep lying to you about obtaining the TSI (stimulating = hyper=Graves') or TBI (blocking=hypo=Hashimotos), and TRAb (TSH Receptor Antibody) so just let it go for now. It's a "cost-effective" move on their part.

Thyroiditis many times can result in hypOthyroidism. By running the antibody testing, it can be determined whether you might have Hashimotos (HYPO) or Graves' (HYPER).

If it is just a temporary inflammation of the thyroid gland, you can be given beta blockers to relieve heart symptoms, and told to get some rest. If the case of thyroiditis is severely hyper, you can be given anti-thyroid drugs. If the thyroiditis is causing hypo problems, you can be given thyroid hormone replacement.

I agree with John that drugs should only be the last resort. There can come a time, though, when you may need the extra help from these -- At least temporarily until you can get your system balanced by correcting nutrient deficiencies and eliminating toxins.

If you think the DOCS have no idea what they're doing when it comes to thyroid disorders, imagine how uninformed the insurance "dictators" are. If your insurance does not cover enough lab testing, you'll never figure out what's wrong with you! In the long run, this ends up costing the insurers even more. Go figure!

Some people get temporarily inflamed thyroids, due to many different causes. But most of the time "thyroiditis" is a catch-all term used by docs who don't really have a clue as to what is going on with you.

Just to prove that the medical establishment does a lot of GUESSING ---- I was diagnosed with Graves' in

1979. In 1997 I was diagnosed as having "chronic thyroiditis" - and this was all with NO PRIOR ANTIBODY TESTING...

Here are a couple of "medical establishment" links. Ignore their "treatment options" but these pages have a lot of info about THYROIDITIS itself:

-

[<http://www.mythyroid.com/thyroiditis.htm>](http://www.mythyroid.com/thyroiditis.htm)

-

[<http://www.endocrineweb.com/thyroiditis.html>](http://www.endocrineweb.com/thyroiditis.html)

Best Wishes, Chris

Re: newest test results/my doctors a moron !

From: Christine
T1: tnccline@prodigy.net
Remote User:

Comments

Hi Retta -

Yes, it took a LOT of restraint! Hahaha!

If you've been on 25 a day for 5 weeks, 20 a day should be fine. You'd probably even do well dropping it to 15. Just find a way to keep checking your thyroid levels to keep on top of the situation. You can't always tell by the symptoms.

You know, it may depend on how long a person has been on the Tapazole as to whether it needs to be very gradually lowered, or can be lowered at a faster pace. All you can do is see what works best for you, and what your thyroid will tolerate. Hopefully, you'll be able to drop it completely when you get your system balanced.

So glad to see your thyroid is going in the right direction. Eventually you will find just the right doctor!

Best Wishes, Chris

Re: newest test results/my doctors a moron !

From: Christine
T1: tnccline@prodigy.net
Remote User:

Comments

The above post holds the inference that the patient will be required to contact a medical doctor in order to obtain bloodwork to determine the thyroid hormone levels, which is referred to as "a way to keep checking your thyroid levels".

When the test results are revealed to the patient, the physician is required to discuss any necessary dosage changes of the medications he prescribes. The patient should be entitled to make changes that will be in his best interests, and promote his well-being.

Chris

Re: newest test results/my doctors a moron !

From: Christine
T1: tnccline@prodigy.net
Remote User:

Comments

Hi Ellen -

I tried to stay away from this thread because if I get started on what morons some of these docs are.....

Anyway -

If you're taking 30 mg a day of Tap (equivalent to 300 a day of PTU), that is a fairly high amount. Your thyroid has become dependent on this "braking" mechanism to keep it from producing too much hormone. To SUDDENLY stop taking it altogether could possibly shock the thyroid and signal it to start overproducing again, regardless of how low the levels have become while on this amount of Tap.

Many of us have had success with lowering it in small increments. If you take small steps to lower it, I wouldn't call that SUDDENLY lowering the amount.

I have lowered the amount too fast before and regretted it. I had below normal thyroid levels on 15 mg a day of Tap. I was instructed to lower it to 10 mg a day for 3 wks, then to 5 mg a day for 3 wks. By the 5th week, my thyroid had shot up (total T-4 was 24, lab range 4.5 to 12)!

I got my thyroid back down to below normal again and the next time I tried lowering the Tap, I took it slow and easy--lowering it just a few mgs every 6 wks or so.

I was able to settle in at 3 mgs a day total, and my thyroid levels stayed on an even keel. They were just about to stabilize in the middle of the normal range, but something has started aggravating my thyroid again. Have increased it back up to 6 mg per day (2 mg - 3 times a day) until I can figure out what went wrong.

Say you are taking 10 mg, 3 times a day--a nice even flow of medication. When you want to start lowering the dosage, you can order the 5 mg pills because it is easier to taper off with these smaller doses.

Then take 1 and 1/2 of the 5 mg pills (they're scored for easier dividing). That would be 7-1/2 mg, 3 times a day. Now you've gone from 30 mg total per day, down to 22-1/2 mg total per day.

The next safe step, after several weeks, and if your test results still show low thyroid levels, you can ease on down to 5 mg, 3 times a day--a total of 15 mg per day.

If your levels are still too low, because you are getting your system balanced or for whatever reason, and you need even less Tapazole you can get creative and split up the dosages even more. Or you can see if taking it once or twice a day works for you.

I do much better taking 3 equal amounts of Tap, every 8 hours, but everyone is different.

Also take into consideration your nutritional changes. You can gradually wean yourself off the Tapazole or PTU while balancing your system. Just make sure you get tested often enough to keep track of your thyroid levels. This way they won't catch you off guard if they start climbing back up again.

If your doctor thinks this is too much trouble for HIM, then find a doc who is interested in helping his PATIENTS, not helping himself and his wallet.

I find that the more "highly recommended" an endo is, the more pompous, insensitive, nuke-happy, and downright useless he/she turns out to be.....

Keep up the good fight, my fellow thyroid-ites!!

All my best, Chris

Re: newest test results/my doctors a moron !

From: Ellen Fix
T1: efix@pcdi.com
Remote User:

Comments

Christine--

I daresay if a medical doctor or pharmacist read your dosage suggestions for TAP, they'd accuse you of practicing medicine without a license. However, I will DEFINITELY ask my new doc about his tapering recommendations--and I will specifically refer to your suggestions. Very helpful; thanks! And one day, dare I predict that Tapazole will be an over-the-counter medication, so we can all be granted the "legal" control of it?

P.S. It sounds like what you're saying is, the longer you've been on TAP, the longer you should take to

taper it off, is this correct?

Re: newest test results/my doctors a moron !

From: Christine
T1: tnccline@prodigy.net
Remote User:

Comments

Hi Ellen -

How many doctors are practicing medicine WITH a license and destroying people's lives due to ignorance and incompetence?

I try to be careful to mention these dosage changes (and any other observations) are based on personal experience. I also try to recommend that you run these changes by your doctor just to cover yourself.

We should all do this when we post suggestions. Many BB's won't even discuss lab test results, much less med changes. But think about it..... If you COULD ask your doctor AND actually get a truthful, unbiased answer out of him, why would you search elsewhere for answers?

Again - Thank you John so very much. You have been a real blessing to us. If I'd missed finding you, I'd still be stumbling around in the dark, fighting with one doctor after another, and never really getting anywhere. Thanks to your courage and your dedication to helping others, many lives have been greatly improved.

We are so fortunate that John provides a place where we can exchange ideas without being censored to death. A place where we can LEARN how to overcome this disease, without the nuke, cut, and poison allopathic mentality.

I'm certain most of the medical profession would consider me to be certifiably nutty, raving lunatic anyway, but I've had enough training in basic law that I usually provide a disclaimer of some kind in my posts. John has also placed a prominent disclaimer on his homepage.

It would be a heck of a lot easier to just sit back and let the doctors pull the wool over our eyes. However, we all take the time to contribute our experiences and theories here, because there is a better way.

Tap dosage lowering:

I consider a medication as a crutch of sorts. It's just a hunch that the longer you've been on a certain medication---as with using a crutch---the more accustomed the body has become to it. If you were to suddenly knock a crutch out from under someone, he may stagger and fall. If he gradually uses the crutch less and less, he will be better able to stand on his own as he improves.

If you try to discuss tapering off the Tapazole with your typical medical doctor, most will have no idea what you're talking about. To most of the docs I've run into, Tapazole is a dirty word anyway!

Many people can take this med once a day. We are also told that we can just drop the meds rapidly, or even cold turkey, but I find this may not work with some people.

Once I was advised to take 15 mg of Tap on one day, and 10 mg the next - alternating. By the 3rd day of this regimen, I was having frequent tachycardia spells (rapid, jackhammer-type heart beats). I discovered this uneven "feed" of Tap was the culprit.

It is a potent medication, and you must find the best application of it for your own system.

I certify that I am not a doctor, and none of this is to be construed as medical advice.... just personal experiences of my own, what I've learned from others' experiences.....

And just plain common sense--rarely found in a doctor's office. <)80)

Yes, let's hear it for over-the-counter Tap, PTU, and replacement hormone. And don't forget home testing of thyroid levels. And an even taller order: Doctors who are required to take nutrition courses.....

It has to be a possibility in the future! We need Dr. McCoy!

All the best, Chris

Long-Term AntiThyroid Drugs for Hyperthyroidism

From: Christine
T1: tnccline@prodigy.net
Remote User:

Comments

Hello Everyone!

This is lengthy, but I hope it can help some of you with questions about this. Was pleased to find the posts below by Ellen, Min, Beth, Cas and Maribeth on the subject of long-term Tapazole use.

I've taken varying doses of this drug for over 22 years now, and have had NO problems with it whatsoever. My only obstacles were dealing with narrow-minded, short-sighted, ignorant, arrogant, incompetent doctors. If nothing else, it has taught me endurance! Don't get me wrong - there ARE kind, compassionate, reasonable doctors out there, but unfortunately these are few and far between.

Once a patient is diagnosed hyperthyroid (based on THYROID LEVELS T-4 and T-3 testing - rather than just a low TSH) he/she needs to bring the thyroid levels down as soon as possible. There are a number of serious health problems that can develop if your thyroid is out of control and goes unchecked. Don't mess around with this!

Hopefully just making changes to your diet and lifestyle will get your thyroid on the right track, but don't discount the value of using the ATD's if your thyroid levels are too high, and you are having difficult symptoms.

Sometimes discovering the changes you need to make, and getting results from these changes might take longer than anticipated. It's easier to balance your system back into health if your thyroid is at a fairly normal level. Not to mention that deciding which changes to make, and keeping track of these changes, is easier if your brain's working correctly.....

Tapazole and PTU (the drugs offered in the U.S.) are generally safe if used correctly, and can bring your levels down to normal in a relatively short period of time. Once your thyroid levels (T-4 and T-3) start to normalize, you'll begin to feel better.

WHAT'S WITH THE TSH?

If the doctor gets upset over a TSH that stays too low, tell him to get over it, as it does NOT matter. Who really knows how long, or how often, you've had a suppressed TSH anyway?

I understand that if one can maintain the thyroid at an ideal, steady level for a substantial length of time, the TSH will seek out its correct level. Who's to say that the TSH "normal range" currently in use is an etched-in-stone fact of life.....?

Since continually suppressed TSH function has rarely--if at all--been studied, there seems to be no data out there to confirm anything one way or another. What's to say whether or not a low TSH, in and of itself, is a problem? Especially a low TSH coupled with perfect thyroid levels? Hmmm?

Due to the common practice of destroying the thyroid (often based on a low TSH reading, no less) few TSH's have been left at low, or even "non-existent" levels.

By the way, it IS feasible to gradually attempt a remission with a "non-existent" TSH level.

Watch the T-4 and T-3 levels, and see how you are feeling. Take notes! Make a chart! List your symptoms, lab test results, and changes in medications. Work on finding a level that is right for YOU.

With the info here on John's fabulous website, as well as some of the other more progressive sites out there, you'll get to the point where you'll need less and less of the ATD as you correct the cause of your thyroid dysfunction. Some of us may accomplish this in a few weeks or months. Others may take longer, depending upon the situation. After all, we are "individuals."

If you're having heart irregularities, there are beta blockers that work wonders, and you can taper off of all these meds once the thyroid gets under control.

It's senseless to put a time frame on ATD use. I can testify that Tapazole can be taken very, very long term, if necessary --- with no side effects. And hopefully soon, I may be able to say that you can achieve remission when you hit on the right formula to straighten out a misbehaved thyroid, regardless of how long you've been on ATD's.

Even though there is a wealth of information on this site, there's still a lot of guesswork involved in custom-tailoring it to each individual person. It can be hit and miss at times. What works for one person may be totally wrong for the next. It might get discouraging at times, but absolutely elating when you reach a goal. Just remember:

Foolishness means doing the SAME thing over and over, expecting a DIFFERENT result each time. Go for it and MAKE SOME CHANGES!

I've had to make major changes in my diet. And learning from the experiences of many of you, I've personally improved in leaps and bounds by eliminating all gluten and dietary yeast.

WEANING OFF THE TAP -

In my case, I seem to have better control over adjusting the thyroid levels while reducing the Tap by taking it in equal doses every 8 hours. This time I have TAPERED SLOWLY, and have had the THYROID LEVELS (not TSH) TESTED FREQUENTLY.

Over the past few months I've been able to taper the Tapazole down from 15 mg a day (5 mg - 3 times a day), to 12 mg, to 9 mg, to 7-1/2 mg, to 6 mg, to 4-1/2, to the the current 3 mg - each split into 3 equal doses, every 8 hours. I may or may not be able to totally discard the Tap, but I'm very encouraged just to get by on 3 mg a day.

I'm certain that others may not need to go to such extremes - once or twice a day dosing might work for some. But if a quick, uneven dose reduction has failed in

the past, the 3 times a day dosing might be worth a try.

(If you have a tough time figuring out how to split it this fine, there are pharmacies that are willing to "compound" a prescription. This means they can custom mix any dosage you might need.)

If a doctor has you on, say, 15, 20 or 30 mgs a day of Tap, and tells you to just drop the ATD cold turkey, there's a chance your levels might skyrocket. Any type of shock to the system like that can have poor results.

I've also seen where some patients are initially prescribed such a high dose of Tap or PTU that they develop side effects, which can be resolved when the dosage is reduced. Or a patient is prescribed a very high dose, and told to come back in 6 months. Say what?? There's always a chance that by being overmedicated--even for a short period of time--you can become so HYPO that you feel like a zombie!

***** You you might NEED to be tested as often as every 3 or 4 weeks when adjusting the ATD dosage. You must have your thyroid levels (T-4 and T-3 -- BOTH) tested often so the meds can be adjusted to keep you at a level that is right for your system. It generally takes 7 to 10 days for a Tap dosage change to make a difference. And a few weeks to "settle in" - but then again, there are no set rules.

ATD's AROUND THE WORLD:

In many other countries, the ATD's are effectively used to control the thyroid. The chance of spontaneous remission can run from 40 to 50 percent within the first year:

Read all about it in the doctors' own words - this is from the New England Journal of Medicine, 1996:

<http://www.nejm.org/content/1996/0334/0004/0265.asp>>

The valuable advice on John's website can and does work - but it might take some time to see results. Since each one of us is different, we each need to find what our own bodies require in order to achieve the correct BALANCE. If you're willing to put forth the effort, success can be yours. As you bring your body back into balance, you will be able to taper off the ATD's while clearing up your thyroid problems.

Some of us may only need to make minor changes. It can be a challenge, trying to figure out your nutritional imbalances, and toxins, etc., but get into this website and READ! If it's all too much for you, then PLEASE..... at least refuse to let the doctors con you into a *rush job* to destroy your thyroid -- with no regard (or guarantee) for your health afterwards.....

So, the athletic-types may need to tone it down for a while. Vegetarians may need to eat some chicken and fish, and grab a burger on occasion. The high-carb pasta and bread fans might try cutting out gluten for a bit (especially if you're having digestive problems... yikes!). Or if you've just gone through a pregnancy, you may have to deal with this temporarily, and it might clear up on its own. We're just beginning to understand the wide array of causes. John has gone above and beyond the call of duty here.

Just try one or two things at first, then gradually work your way down the list. For starters, you might add selenium and copper to your diet(supplements or food sources - they both work), acidophilus, more protein.

This is a great bunch of friendly, helpful people. Don't know where I'd be without you all!

Warmest Regards, Chris

[tsh levels](#)

From: Lynn
T1: barnesjt@chartermi.net
Remote User:

[Comments](#)

Hello! My last blood test showed my tsh level at .03, is the normal range from .23 to .5 or .23 to 5.0? Is .03 really hyperthyroid or borderline? I started off with eye problems and thyroid levels were fine. I quit smoking and my thyroid levels went hypothyroid 6 months later. I started smoking the same day they put me on synthroid. I am now hyperthyroid. My doctor wants me to have rai uptake and scan done. I asked my eye doctor if this would affect my eyes and he said no. He would be more worried about them if they put me on tapazol or something like that. I have the hair analysis done and am taking Johns advice for supplements. I am not having any problems with my eyes or my body right now. Except I get a little warm, but not bad and my stool have been loose for three years. Could this tsh level of .03 be affecting other organs in my body that I may not be aware of? Some advice please! Will this rai scan show if I have cancer of the thyroid. Would this have shown up on an ultrasound which I have already had? I feel like I have 100 people telling me to have the scan and 100 people telling me not to. Stuck in the middle and way confused. I don't mind waiting to have the scan done if it isn't affecting anything else like my eyes. Once the eyes start it is too late and just a matter of waiting it out. Thanks for listening and would appreciate any help

From: Christine
T1: tnccline@prodigy.net
Remote User:

[Comments](#)

Hi Lynn -

I've tried to answer your questions below. This will give you some general guidelines in dealing with your medical care provider:

>>>>My last blood test showed my tsh level at .03, is the normal range from .23 to .5 or .23 to 5.0?

--- Generally to 5.0, but many feel too hypo at that high of a TSH, even though it is still considered normal. Most people do well at a TSH level of 1.0 to 2.0, or even lower.

>>>>Is .03 really hyperthyroid or borderline?

--- 0.03 is considered a below normal, suppressed or "non-existent" TSH level.

TSH can be suppressed if thyroid levels are normal, borderline, or hyperthyroid. I've seen TSH suppressed even while hypothyroid.

>>>>I started off with eye problems and thyroid levels were fine. I quit smoking and my thyroid levels went hypothyroid 6 months later.

--- Are you saying that your thyroid levels were fine 6 months ago (were you tested then)? Also, what caused you to become hypothyroid 6 months later? Was this confirmed by recent blood tests?

>>>I started smoking the same day they put me on synthroid. I am now hyperthyroid.

--- Are you still on synthroid? Taking synthroid when unnecessary could explain not only the hyperthyroidism, but also the low TSH.

Have you ever taken tapazole or PTU? Have you ever been given beta blockers?

>>>My doctor wants me to have rai uptake and scan done.

--- Why? What are they trying to find out? What were the results of the ultrasound? Get a copy.

>>>Would this have shown up on an ultrasound which I have already had?

--- Didn't they even tell you the results of the ultrasound?

>>>I asked my eye doctor if this [RAIU] would affect my eyes and he said no.

--- No one knows for sure either way as there are no long term studies.

>>>He would be more worried about them if they put me on tapazol or something like that.

--- What does your eye doctor know about tapazole? Probably a bunch of old wives' tales that circulate through the medical world. Actually we've seen a tendency for Tapazole therapy to have a protective effect on the eyes.

>>>I have the hair analysis done and am taking Johns advice for supplements. I am not having any problems with my eyes or my body right now.

--- Since you are having no bothersome symptoms, and I assume a normal heart rate, why do they want the RAIU testing? If they want to determine which type of thyroid disorder you have, this can be done with blood tests, and save you the nuclear exposure.

If the .03 TSH is the only problem, and your thyroid levels come back as normal, and you are having no symptoms -
- then do nothing and keep monitoring your thyroid levels over the next several months.

Try to get a T-4 and T-3 every few weeks or so, and demand a thyroid levels test immediately if you start feeling bothersome hyper symptoms.

You need a "free" or "total" T-4, and "free" or "total" T-3 right now. Note: A T-3 Uptake is not a measure of the T-3 hormone.

Once you get CURRENT THYROID results, you'll know just how hyper or hypo you are..... and can go from there. The TSH can remain suppressed at 0.03 for months after thyroid levels become normal, so that a TSH level by itself tells you nothing.

If you've been hyper for a while, the TSH could take longer to normalize after thyroid levels are normal.

>>>Could this tsh level of .03 be affecting other organs in my body that I may not be aware of?

--- No one knows for sure, but it doesn't seem to cause problems. In fact, many times the TSH is suppressed on purpose, as a therapeutic measure in certain cases, to aid in controlling nodule size.

>>>Will this rai scan show if I have cancer of the thyroid.

--- No, it might denote density of different thyroid tissues, but it won't differentiate cancerous cells from benign.

An ultrasound will show nodules, and an FNA (fine needle aspiration) biopsy can help determine the condition of the contents of any suspicious nodules. However, many times the biopsy results are "inconclusive" and you're right back where you started--with no answers. However, nodules are usually benign.

>>>Once the eyes start it is too late and just a matter of waiting it out.

-- The eye involvement is usually caused by antibodies attacking the eyes. Sometimes it can even be independent of the thyroid disorder.

You never can tell which direction the eye condition will take. There's always the possibility that the eyes can improve once you get the thyroid situation straightened out.

Hope this helps some, Chris

[Christine](#)

From: Lynn

T1: Barnesjt@chartermi.net

Remote User:

[Comments](#)

Hi Christine. Thanks for taking the time.

Basically in Sept 1998 my eye popped out. Thyroid levels were normal, but thyroid stimulating immunoglobulin was elevated indicating I had graves disease. Doctors did not do anything at that time.

I quit smoking and by February of 2000 my thyroid levels went hypothyroid and I was put on .05 of synthroid.

By July of 2000 very depressed and levels indicated I needed more synthroid. I started taking .088 synthroid and starting smoking same day.

By January of 2001 started getting too much synthroid and they lowered me to .075.

February 2001 lowered again to .05.

March quit taking synthroid all together.

July of 2001 my TSH was .03 and t4 was about 11.9 and in

Sept of 2001 my TSH was .03 and t4 was 10.6.

I think my doctor wants to do the uptake scan cause he wants to zap my thyroid-not sure. He is in marshfield and ordered the test.

He told my I and two thyroid disorders. One was working on making me hypothyroid and the other disorder was working on making me hyperthyroid and it was a matter of which one won out.

Well when I went low thyroid he told me it would be very rare to hyperthyroid again. Well, I guess I am rare!

Feeling great, but my left eye does seem to be swelling some where it was initially my right eye.

I would not get this test done, but I am worried that the ups and downs of my thyroid may cause me more problems. I know if if they zap my thryoid it won't help my eyes because it is seperate, but my eyes may not start active again if I zap my thyroid and keep it from going hyper and hypo and hyper and hypo. Do you know what I mean?

If I could call you sometime that would be great. If you didn't mind maybe you could leave your number on my e-mail and let me know a good time. If you get a chance please respond to this as my appointment is October 25. Its okay if I can't call you, but I sure appreciate your help. Its hard to get it all written down right on here. Have a good day. Lynn Barnes

Re: Please Help Me Make Sense of My Test Results!!

From: Suzanne

T1: sroloff1@home.com

Nov.17, 2001

Comments

Becky, Welcome, you have come to the right place, I think. I cannot help with exact things on testing and numbers, and it depends on the normal ranges for your lab, so maybe someone else can help with that. But if you are hyper, have candida and chemical sensitivities, I can help a bit with that.

First, I think it all goes together and involves the immune system, and an overburdened one at that! I assume the drug you are taking is for the rapid heart rate, so stay on that. What also helps with that is calcium and magnesium, probably more magnesium at first than calcium, so you would have to buy them separately. Magnesium helps to slow the heart rate down. B complex is also helpful and at first you may need a lot, like anywhere from 3-6 a day. I would start with these two things and also buy some copper and start with 3-5 mg. of copper a day and see how you feel. Most hypers are deficient in copper. You may also need some additional separate b vitamins like boron or papa or biotin, but just to keep things simple start with the b complex first. Keep a diary of how you feel and what you have added, etc. As far as the candida goes, it is essential to change your diet and become informed of the disease. It can reak havoc with your whole system and organs and can be quite detrimental. You have to starve the yeast by changing your diet and taking supplements to kill the yeast. There are many different ones and you can change taking them every couple of months, they are garlic and onions, olive leaf extract, oil of oregano, caprylic acid, biotin, pau du arco, rosemary and thyme, and many others, but you can start with a couple of those. You also need to take probiotics to repopulate the good bacteria again, that is essential and you need to take it in the morning and at night for a very long time, if not forever, if you have a bad case of the candida. As far as diet goes, an anticandida diet is good for thyroid, too. You need to focus on good quality protein, organic without hormones or pesticides or

chemicals, vegetables, nuts and seeds, and a little fruit, but not the high sugar kind in the beginning because of the candida. Candida feeds off of sugar and yeast and mold, so no cheese, breads, or sugar of any kind. It is a tough diet, but if you can stick with it for several months you will notice a drastic difference in your health. There are two good books you might want to look into about candida, they are "The Yeast Connection and the Woman", by William Crook, and "The Body Ecology Book", by Donna Gates. There are many things you can do naturally for chemical exposure, too. You didn't say how you got it, the first thing would be to get rid of the exposure of course. Depending on what chemicals they are, there are different things that help chelate the chemicals out of your body. I know that Vit. C and garlic are two, and that would help with the candida, too. There are many websites where you can look up about chemical problems and what to do about them. You have to be careful though, because you can get very sick ridding them from your system. I would recommend doing this through a naturopath physician, especially if you are very sick. The thyroid and candida you can work on yourself though. You still may get detox and feel sick as you are ridding yourself of the candida, but it is not as bad as the chemicals.

I myself have dealt with all three of these problems in the last several years, and was also very sick when I started, but I am finally fine now, but it was a lot of work and change on my part. You can get better though, and without drugs. Your system does not need any extra unnecessary drugs at this point.

There is lots of support here and information on the main page of this site, John talks about all of these issues, too.

Let us know how things go for you.

Suzanne

Dec. 6, 2001

From: Beth

T1:

Remote User:

Comments

Hot sauce helps my sinuses. Do you have any tobasco sauce or cayenne pepper?

A hefty dose of cayenne in a cup of chicken soup works wonders! :-)

Horseradish also helps, I'm told. A friend of mine juices it and it helps her allergies/sinus.

Jan. 8, 2002

Stainless steel leaching

From: Greg Marlow

T1: marlowgs@altavista.com

Remote User:

Comments

To All,

I read John's page on drinking water and would like to tell you what I have discovered. Recently I stopped using stainless steel cookware and a stainless steel water distillation apparatus and my hyperthyroid like symptoms disappeared almost overnight. My internet research leads me to believe that toxic levels of nickel were being leached from the stainless steel. I hope this will be of some assistance

From: John

T1: BU007@aol.com

Remote User:

Comments

Hi Francine,

I'm sorry to hear about all of your health problems, but I think it's possible to sort it out and get your health back. The fact that you have four daughters with health problems may be helpful, since you can get hair analyses of everyone to determine what deficiencies and toxicities you all have in common.

It's possible that besides being deficient in certain nutrients, you are all being poisoned by something in your environment or food. You mentioned that you have very high barium and this is particularly bad. Many people get barium toxicity from barium enemas for medical radiographic analyses. Also, barium is the toxic agent in rat poison. Barium is a very strong antagonist of potassium, so ingestion of barium causes low potassium and this can lead to death as the respiratory and heart muscles lock up. This is how rat poison works on rats. Generally in people potassium gets very low, you gain weight (water), your joints and muscles get less flexible, and your cells have a reduced ability to take up minerals. You need to find out where the barium toxicity is coming from and find out if

the other members of your family also have this problem. In the meantime, eating a diet high in potassium should help.

The supplement that the naturopath recommended is not a complete multiple supplement so it may have helped you initially if you were deficient in the nutrients that it provided, but eventually supplementing only some nutrients will unbalance your other nutrients and lead to other deficiencies. This is especially true of the B complex vitamins. Taking B2 and B5 will deplete you of B6 (sore joints, especially the wrists; low zinc metabolism with subsequent hypothyroidism), B1 (itchy ears and eyes; high fears and inability to deal with stress), and B3 (sore tongue, anemia, many other problems). You'll need to make sure that you are getting all essential nutrients so that you aren't getting depleted in some of them.

I don't know if you are grinding your own grains for breads and other consumption, but it's very easy to get heavy metal toxicity from grain grinders, even commercial ones. The metals and stones used to grind grains into flours can impart heavy metals like cadmium which has strong effects in depleting copper, zinc, selenium, and other minerals. I think it's best to avoid all grains except whole grains. Avoid rice because it grows in swamps where cadmium accumulates. Plant leaves accumulate cadmium and these wash down into swampy areas where growing plants take up the cadmium. Among the grains, oatmeal doesn't seem to be too bad, perhaps because it is rolled and not ground. The best thing is to eat a diet of primarily meat, eggs, beans, nuts, seeds, and vegetables, with a very few fruits.

If you'd like to send me copies of whatever hair analyses you have for your family members, you can send them to John Johnson, 31275 La Baya Drive, Westlake Village, CA 91362. If they are clear you can fax them to (818)889-6969. Please list ages and symptoms for each person. Hopefully we'll be able to start getting your family back on track. John

Note re TSI

From: Christine
T1: tnccline@prodigy.net
Remote User:

Comments

Just to clarify:

If the TSI (Thyroid Stimulating Immunoglobulins) is elevated, it means you have the "stimulating" antibodies and have Graves' disease. If the TSI is negative, it means you probably don't have "active" Graves'. But it doesn't tell if your thyroid levels are high or low at the moment. You could have either "inactive" Graves' or simple hyperthyroidism and still have a negative TSI.

In order to have full diagnostic testing of this sort, you should also have a TSH receptor antibody test run. Otherwise, this testing is incomplete.

Chris

Re: Amalgam Fillings / Mercury

From: Mae
T1: Shoepi58@gw.total-web.net
Remote User:

Comments

Hi! I am in the process of having my mercury fillings removed to see if it will help me with hyperthyroidism and allergies. My dentist told me to take dl-Methionine supplement which is supposed to help rid tissues and organs of mercury. The supplement has the brand name of Redoxal HMF and is manufactured in Ga. Doc said it is an amino acid which binds with mercury?? Since I started taking it. I have seen improvement in some excema that I have had for years. Good luck!!

From: John
T1: BU007@aol.com
Remote User:

Comments

Hi Suzanne,

Getting enough iron is difficult for many people. This is probably why iron deficiency is still the number one nutritional deficiency world-wide.

Iron absorption from foods is very limited. The Nutrition Almanac states that only 2 to 10% of the iron in beans, fruits, and vegetables is absorbed. Animal sources of iron are better absorbed. While the body can use several forms

of iron, such as ferric or ferrous iron (ferrous is better), the best form is heme iron. Actually heme iron makes other forms of iron more absorbable, so it's probably best to take an iron supplement with a meal of red meat.

Some things can interfere with iron absorption. Lack of hydrochloric acid in the stomach is a big reason. Person on a low salt diet might not be getting enough chlorine (the Cl in NaCl) and therefore not able to produce enough HCl. Taking a good digestive enzyme with the iron supplement should assist the absorption.

Too high an alkaline diet might interfere since iron needs an acid environment. Eat more acid foods with your iron. Too much roughage in the diet can speed up intestinal transit time and reduce iron absorption. Too much coffee, tea, phytates (from grains), oxalates (spinach, rhubarb), and phosphates can all interfere with iron absorption.

There are nutrients which need to be present for iron absorption: B-12 (try a high potency, 3000 mcg); folic acid (400-800 mcg); vitamin C (1000 mgs); vitamin A; copper; calcium; manganese; molybdenum; and other of the B complex vitamins.

Excessive intake of vitamin E and zinc can interfere with iron absorption. Vitamin E in amounts like 800-1000 IU per day can cause iron deficiency (causing ear aches). Don't take more zinc than iron, since that can also deplete iron.

If all else fails, you might want to experiment with different levels of the B vitamins. It may be that you need more B vitamins and need to get up the the 200 mgs per day quantity. However, I'd try the other things first.

Bulletin Board

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Re: Amalgam Fillings / Mercury

From: Cathy
T1:
Remote User:

Comments

Call DAMS (Dental Amalgam Mercury Syndrome) at 1-800-311-6265 and ask for their excellent information booklet. You can also get references from them.

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To Lisianthus

From: Christine
T1: tncceline@prodigy.net
Remote User:

Comments

Hi Lisianthus -

I'm a little confused on this. Are you saying that they put you on PTU (anti-thyroid hormone) based on a test from 4 weeks ago? Why did it take them a month to let you know the results??? Why did they give you PTU when these most recent test results indicated hypO? And now they have you on thyroid hormone replacement? Does your doctor have any idea what he's doing? It takes a typical medical lab about 3 hours to run both "free" and "total" T-4 testing, "total" T-3 and TSH. Why on earth are they basing your medication on a test that is 4 weeks old? Sounds like these guys are just guessing. Get your thyroid levels tested again as soon as possible. And make sure you get the results by the next day If you go to the local hospital lab, you can usually get the results within 3 hours. Your doctor is probably on staff at a local hospital and can arrange for this. INSIST ON IT! It isn't surprising that the supps have worked this well, this fast. I wonder if you could benefit from a TBI (thyroid blocking immunoglobulin) test, which can show if there are antibodies that correspond with hypothyroidism. Also get the TSH receptor antibody test.

Best Wishes, Chris

Re: Postpartum, Lactating, Hyperthyroid

From: John
T1: BU007@aol.com
Remote User:

Comments

Hi Stephanie,

Many women get hyperthyroidism in the third trimester or during lactation and this scenario points to a copper deficiency caused by low levels of copper going into a pregnancy or the use of high iron supplements (most prenatal) during pregnancy.

Being thin is a sign of copper deficiency. Even though you may have always been that thin, this does not mean that you are healthy. At 5'6" you should weigh at least 120 pounds if you are small-boned and thin. Being under 110 is an indication of malnutrition. Both being thin and not gaining at least 25 pounds during pregnancy are indications of copper deficiency.

Another sign of copper deficiency is feeling hot. When copper is low, excess iron forms excess norepinephrine which is the heat producing catecholamine hormone. Taking copper will cool you off since it enables the body to use the iron to form hemoglobin instead of norepi.

Some women have found that stopping nursing will end the hyper symptoms. I don't think this is the best way, since it's better to nurse your baby. The best thing is to replenish your copper and other minerals and nutrients so that you can provide these to your baby in addition to recovering your own health. If you don't supplement to correct your deficiencies, then it's better to give your baby milk from healthy cows or goats rather than your nutrient-deficient milk.

The one mineral that baby's drain the most from their mothers is copper. The baby has to be able to live for up to two years on the copper that it obtains during gestation. This is why copper deficiency is so common during pregnancy and right afterward.

I would recommend definitely avoiding the RAIU and, of course, RAI. Since your TSH is already high, it looks like you are taking too much PTU. You should consider decreasing this to avoid being hypo and at the same time, supplement with copper and the other nutrients for hypers.

At your age you should be able to correct these nutritional problems quite quickly.

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Thyroiditis, Schmyroiditis.....

From: Christine
T1: tnccline@prodigy.net
Remote User:

Comments

Hello Lisianthus -

If this endo/specialist is "hard to talk to" then he's NOT really much of a doctor, is he? If there is no communication between the patient and the doctor, how in the world are you going to get well??

Stick with the PCP, or find another PCP who knows about thyroid disorders. You don't need an endo who lies to you about the testing, keeps guessing about the treatment, and regards you as someone who can easily be jacked around.

From the beginning, it sounds like they've been trying to put you into a squeeze play over this RAIU. Continue to refuse it! Most of what the docs need to know can be done with bloodwork. They DO get mad when you refuse their cheap, toxic, diagnostic testing.

If you haven't already done so, please read the info from John and Elaine on RAIU, accessible from the homepage of this website.

What's going on with this lab test runaround is the old soft-soap routine. "Oh, yeah honey, we'll run those tests. No

problem." Then you get the minimum from the lab, which sadly enough can sometimes be just a TSH. They will run only what they have to and nothing else.

If they based their decision about treatment on just the TSH, they need to go back to school.

First off, you need to ask that they let you see the lab order. Then you can SEE, and make remarks about, what they have ordered.

Even that isn't foolproof, though. I've seen labs refuse to run a blood test as simple as a "total" T-4, because "they never run THAT test" and was given no reason other than that. The doc had marked both "free" and "total" T-4 on the lab request.....

If they refuse to let you see the order, say this:

"Just because I don't have 8 years plus of medical school under my belt, does that make me an ignorant moron? I want to participate in my health because I know my body better than anyone else on earth. If you can't bring yourself to lend me enough credibility and respect to keep me informed, then please direct me to a REAL doctor who will."

OK, you need:

T-4 (both "free" and "total" if you can get them)

Note re T-4 - I've had the "free" T-4 in the "normal" range and the "total" be above normal, so getting both of these can give you more info when you are having symptoms

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Re: Liver damage

From: Caren
T1:
Remote User:

Comments

Hi! There are liver cleanses that you could perhaps try - one I know is - half a (pref. organic Lemon) clove of garlic (minced) and a tablespoon of flax oil taken after getting up. Also, there are herbs that are good for the liver - I THINK Milkthistle is one - but best to see a herbalist or naturopath (or even homeopath). Best wishes Cas.

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Re: Iodine

From: Nancy
T1: nlcpaint@ameritech.net
Remote User:

Comments

I was able to get rid of candida after using Immunogard which I bought from the www.thyrodine.com website. This really worked for me. Before that I had been trying everything my doctor suggested, but still couldn't get rid of it. They are a clinic in New Zealand.

Shellie's Hair Analysis

From: John
T1: BU007@aol.com
Remote User:

Comments

Hi Shellie and Everyone,

Shellie faxed me her hair analysis and told me that she'd like to share the analysis on the bulletin board. Following is her email to me, her hair analysis numbers, and my interpretation.

Hello John, I recently found out I have graves disease and have found your site to be both informative and encouraging. I have enjoyed reading the bulletin and hearing what others have to say about their experiences.

I have been on PTU for 7 weeks and have seen dramatic differences in my T4 levels. I no longer have a racing heartbeat or experience heat intolerance however I have gained 8 lbs which I'm not too happy about.

Results:

April 13-01 TSH .03 lab range .35- 5.50 T4 20.8 lab range 4.5-12.0

after six weeks on 300mg of PTU the lab results:

June 22-01 TSH same Free T4 1.47 lab range .61-1.76 (I only knew to ask for this because of your information) T4 10.6 lab range 4.5-12.0 T3 Uptake 36 lab range 24-39

So as you can see I am very happy about the results and I am thankful to know what to test for.

I was hoping since I'm rather new at this that you would take a look at my hair analysis and give me some idea of how to proceed. I do have a copy of your supplements list and also the "Success Story/Hair Analysis" bulletin dated April 4, 2001.

I guess at first glance I see the deficiencies in Manganese, Zinc, Chromium, and selenium but I'm thrown off by the high levels of copper and potassium.

The good/bad news is I can not get into see an endocrinologist until Sept. So I have some time to start the supplement program. My Primary Physician has already said I can not stay on the medicine indefinitely and may have to go to the next step which I like so many of you am trying to avoid.

Your help would be greatly appreciated and I'd love to share this discussion with others on bulletin board.

Once again thank you for the help you have already provided so many and I'm looking for any guidance you can give.

PS Are you familiar with the Biotics Research Products - and where in all of this do I find my Iodine Results? Should I be concerned about the low WBC in my blood work that indicates a viral infection? Im feeling fine. and finally have you done any work with the levels of toxic metals and how they could possibly relate to hyper/hypos. As you can see from my hair anaysis the aluminum is off the charts.

Thank You

Shellie's mineral analysis (Analytical Research Labs): Calcium 140 (normal 40) (high) Magnesium 11 (6) (high) Sodium 72 (25) (high) Potassium 105 (10) (high) Iron 1.2 (3.5) (low) Copper 3.9 (2.5) (high) Manganese .05 (.20) (low) Zinc 10 (20) (low) Chromium .01 (.12) (low) Selenium .038 (.18) (low) Phosphorus 11 (16) (little low) Lead .27 (ok) Mercury .05 (ok) Cadmium .04 (a little high) Arsenic .012 (ok) Aluminum 4.99 (high) Nickel 1.28 (normal .1)(high) Cobalt .012 (.04) (low) Molybdenum .01 (.11) (low) Lithium .007 (.2) (low)

Interpretation:

Shellie has somewhat complicated situation, since she has many very low minerals that are critically important and high copper.

Most hypers either have very low copper (.8-.12 range) or high copper. Shellie's high copper indicates that copper is not being used properly. This could be because of vitamin deficiencies, like B1, B2, niacin, B5, biotin, or PABA, or because other minerals that work with copper are very low (iron, zinc, chromium, molybdenum), or because of high levels of two copper antagonists (aluminum and nickel).

Most hypers have high levels of aluminum and I suspect that the lack of copper in the cells allows aluminum to accumulate. Shellie's high nickel is unusual. However, nickel, being right next to copper in the Periodic Table (nickel is element number 28, copper 29) is a direct antagonist to copper. Women often get high nickel from nickel plated jewelry (nickel plated posts on ear rings), or working with nickel plated equipment such as in the hairdressing industry). It's possible also that low copper metabolism allows nickel to accumulate and getting enough of the vitamins that work with copper will correct the high nickel problem.

Selenium is important, but it's possible that if Shellie takes selenium she might start converting more T4 to T3 and increase the hyper symptoms. It's difficult to predict but she should try some selenium to see if she can tolerate it. If not, she'll have to get her other minerals up and try again later.

Many hypers have low copper and high zinc, but Shellie has the opposite. It's possible that the copper is not working well because of her low zinc levels, so she'll need to try very small amounts of zinc to see whether this pushes her more hyper or slows down the hyper symptoms. The same is true for iron. Most hypers have to avoid iron at the beginning but she will need to try some iron to see if that helps her copper utilization.

Manganese and chromium work as a pair. When both of these minerals are low, both need to be supplemented. However, sometimes manganese can stimulate thyroid production, so it's best to start chromium first and then introduce manganese cautiously.

Molybdenum should also be tried. Solgar is the only company that I know that makes a molybdenum supplement and any store that carries that brand should be able to special order it for you.

The high levels of calcium, magnesium, sodium, and potassium can be misleading. These levels will come down, but often it's necessary to supplement even though the look high. I would try magnesium, since the cal/mag ratio is high. Avoid calcium foods (dairy) and use magnesium to keep the heart rate lower.

It's going to be tricky finding which minerals will be tolerated. Copper may need to be supplemented even though it looks high. Once you start taking the vitamins that help copper, the excess copper could get used up quite rapidly. You're going to have to experiment with all of these minerals to see which help and which make it worse. It's likely that you may not tolerate some of these minerals at the beginning but will tolerate them once some other minerals increase.

When you try minerals, introduce them one at a time. If you get a negative effect, that can offer hints about what you'll need to try next. Let me know what happens. John

Reflexology

From: Caren
T1:
Remote User:

Comments

Hi! I just wanted to mention to everyone that reflexology can sometimes be helpful for thyroid (and other) problems. And you can do it yourself. The neck area generally seems to be located around the big toe - around the sides especially. So if you massage these areas yourself it may help. Also - the area above, under and all around the bumpy ridge under the big toes corresponds with the thyroid. The top of the toe corresponds with the head and brain - so can be massaged to aid the emotions. Hope this is useful to some people! Love Cas

Success Story/Hair Analysis

From: Deanna
T1: deannam@grwolf.com
Remote User:

Comments

Hi to everyone, I don't post often so here is a refresher about me. March 2000 I was diagnosed with HyperT. Major Symptoms have been rapid heart beat;weight loss;TED;pretibial myxedema;brain fog;muscle weakness;lack of energy;sensitivity to heat and shortness of breath. Having minimal success with herbs and homeopathy, finding this website was all in divine order. I have strong convictions regarding drugs and the ability of doctors to get at the root cause of what goes on with our bodies. Therefore, I taken none and just followed this website.

July 2000 I eagerly dove into the supplementation program, started a high protein low carb diet (previously a vegetarian for 8 yrs) and began daily skilled relaxation program (Qigong). Today I'm here to express my heart felt thanks to John for this incredible Website and everyone who has given the time to share their personal journeys. I believe I was slowly killing myself by the way I was eating, which at the time I thought was healthy and by not managing the stress in my life.

I've put on all the weight that was lost;heart rate is now in 60-70 range resting,80-100 range with everyday stuff like walking and doing laundry, and 120-140 range during my strength training days. Yes, I can finally build muscle without fear of a heart attack! I no longer experience muscle weakness; and lack of energy, sensitivity to heat and shortness of breath is minimal. The pretibial myxedema is 95% gone!!! TED still appears to be a tougher nut to crack. The bulging is much less but I do experience weepy eyes periodically when I lay down or am exposed to the sun--not as red as they used to be.

Listed are the supplements and amounts I've been taking since July. John, I'm faxing you my hair analysis tonight for your review. Boron 6mg. Calcium 400mg. Magnesium 1200mg. Chromium 200mcg. Copper 6-8mg. Iron 28mg. Molybdenum 500 mcg. Selenium 400mcg. Silicon 880 mg. Sulfur 300mg. Vitamin A 20,000 IU D 800 IU B Complex 50 mg. B-1 200 mg. B-2 200 mg. B-3 200 mg. B-5 500 mg. Choline/Inositol 500 mg each Biotin 900mcg. Folic Acid 400mcg. PABA 200 mg. Phosphatidylcholine 2 1200 mg caps E 400 IU Alpha Lipoic Acid 200 mg. L-Lysine 500 mg EPA Natural Fish Oil 2,000 mg. Acidophilus 2 caps Manganese 5mg. weekly Zinc 10mg. weekly Kelp 1 capsule (started 1 week ago)

John, the questions I have are: 1) Based on my heart rate how should I adjust the cal/mag amounts? In the past week I changed to 800 each. What do you think? 2) Is it time to add B6? If so, how much? 3)Should I adjust copper/iron

ratio? 4) How should I adjust the zinc & manganese since I have been taking a very little amt weekly? 5)I've restricted green leafy vegetable to one salad a week. Any problems with increasing to 3-4 times a week? 6)Still have a great deal of puffiness under my eyes, any ideas on this? 7)Is it time to reduce the supplements to a more "normal" amt? What would that be? If not, is there a problem with taking high doses for extended periods of time? 8) Any other recommendations you have?

I apologize for the length of this post. Still have lots of questions and just wanted to share my story--for those who may be discouraged--hang tough, it can work for you!! Thanks again John and everyone--I couldn't have come this far without you.

Deanna

Article on Boron-Chalk another one up for John!

From: Cathy
T1:
Remote User:

Comments

I subscribe to Dr Jonathon Wright's Nutrition and Healing Newsletter and wanted to share with you an article that appears in the July 2001 issue--"Safe and inexpensive boron offers prostate cancer prevention and protection from autoimmune diseases-Although it's too early to say for certain, recent (they don't know about John's site, do they?) research findings indicate that the trace element boron may prevent prostate cancer and autoimmune diseases(lupus, Graves, Hashimoto's, MG, type 1 diabetes,vitiligo and Ms). ...Researchers, from the USDA's Human Nutrition Research Center in Idaho, reported that studies on animals have shown that the equivalent of 2 mg. of boron taken daily prevents the activation of T-helper and T-suppressor cells, both of which are involved in autoimmune disease. These results were significant enough to persuade the researchers to launch a study of supplemental boron as a treatment for rheumatoid arthritis...." There's more to the article but the above contains the parts relevant to this site.

Re: Hyper Relapse/What a Mess

From: Sandy
T1: VenturaGirl@hotmail.com
Remote User:

Comments

Jaw,

I began to take a product called Mineral Rich which interestingly enough contains many of the minerals and vitamins discussed on the supplement end of this site. I also took a whole lot of vitamin C and some E. I had to take 4 or 5 ounces of the Mineral Rich product a day in order to get enough of the minerals and vitamins I seemed to need. The product, as well as many other excellent ones are put out by Maximum Living, and are available in most health food stores.

I don't know if the last episode I had was not as bad as the one I am experiencing now or not,so I can't say for sure just what happened, but I do believe that it is possible to improve the health of the thyroid with nutrition.

Sandy

Re: SOY - good or not good

From: Bonnie
T1: Bmcghee83@aol.com
Remote User:

Comments

Please see below:

Dangers of Genetically Altered Foods

In 1998, Arpad Pusztai, a researcher at Rowett Research Institute in Aberdeen, Scotland, performed the first independent non-industry sponsored study analyzing genetically engineered food and its effects on mammals.

The study had been undertaken to determine whether or not the spliced genes themselves could be damaging to the mammal ingesting them. However, preliminary data from the study suggests something even more startling.

The actual process of genetic alteration itself may cause damage to the mammalian digestive and immune systems.

Pusztai's study found that rats fed transgenic potatoes (artificially bioengineered to include a gene from another species) showed evidence of

organ damage thickening of the small intestine poor brain development

The transgenic potatoes used in the study had been genetically engineered to contain lectin, a sugar binding protein, to make the plants pest-resistant. The adverse reactions only occurred in the group that was fed the transgenic potatoes. The control group, fed plain potatoes mixed with lectin from the same source, were normal.

These results indicated that the adverse reactions were not caused by the added lectin, but by the process of genetic engineering itself. "All the presently used genetically modified material has been created using essentially the same technology, If there really is a problem, it won't just apply to the potatoes, but probably to all other transgenics.

In August 1998 Pusztai appeared on the British television program *The World in Action* to report the findings of his study. In an attempt to quell the resulting public furor, Rowett Institute director Philip James (who had approved Pusztai's TV appearance) said the research didn't exist. He fired Pusztai, broke up his research team, seized the data, and halted six other similar projects.

It came out later that Monsanto, a leading U.S. biotech firm, had given the Rowett Institute a \$224,000 grant prior to Pusztai's interview and subsequent firing.

Evidence emerged to support the legitimacy of Pusztai's research. The research that James claimed did not exist showed up during an internal audit. Later, *Lancet*, the prestigious British medical journal, published a peer-reviewed paper Pusztai had co-authored supporting the research.

Prince Charles began to question the safety of genetically engineered foods on his website and became allies with Pusztai. Charles wrote an article in the *Daily Mail* expressing concerns over the lack of prerelease safety research on genetically engineered foods.

Back in 1992 the U.S. Food and Drug Administration had determined that genetically engineered foods were in most cases "the same as or substantially similar to substances commonly found in food" and thus are not required to undergo specific safety tests prior to entering the market.

The FDA's policy was a dramatic shift away from the long- standing requirement that companies prove their products are safe. Says Rebecca Goldberg of the Environmental Defense Fund. "FDA's policy strongly favors food manufacturers at the expense of consumer protection."

According to author Ben Lilliston, no independent or government-sponsored research into the effects of genetically engineered foods on mammals is now being carried out in either the United Kingdom or the United States.

Update by Ben Lilliston (blilliston@iatp.org)

Genetically engineered crops have been introduced in the U.S. in a quiet, almost stealthy manner. Most Americans know little about this radically new way of producing food, and even less about what type of risks these foods pose. Traditionally, U.S. regulatory agencies are some of the toughest in the world in protecting human health and the environment.

But, as the article points out, genetically engineered foods have entered the marketplace almost entirely unregulated.

The story was published at the beginning of a turbulent year for the biotech industry. For the first time since engineered crops have been introduced, we saw a decline in the overall planting of GE crops in the U.S. In response to growing domestic and international criticism, the Food and Drug Administration announced it was drafting new rules for regulating these crops.

Perhaps the most important event in the last year was the contamination of the food supply with the unapproved genetically engineered StarLink corn. The corn had been approved by the Environmental Protection Agency for consumption by animals but not humans, because of concerns that it may cause allergic reactions.

The StarLink discovery by a coalition of advocacy groups has resulted in approximately 300 food products recalled, mass litigation within the agriculture community, and drops in exports to key markets including Japan. StarLink has also raised questions about the U.S. regulatory system, and, at the end of 2000, several bills in Congress were proposing major changes in the way U.S. agencies regulate these crops.

The last year has seen dramatic changes within the agriculture community regarding GE crops. Farmers are now having to worry about liability, markets, and cross pollination. Grain elevators are facing increased expenses associated with testing and segregating genetically engineered and non-GE crops.

And even giant grain processors like Archer Daniels Midland are warning farmers about growing genetically engineered crops.

The entire food sector is wary of the impacts these crops are having on our ability to export.

The mainstream media has been consistently behind the ball on the story of genetically engineered crops- particularly the regulatory angle. While they have been quick to cover the latest scientific breakthroughs by the industry, and report extensively on the promise of the technology, they have ignored the inability of U.S. regulatory agencies to keep up with the advances and unique risks of biotech foods.

While the StarLink debacle has received considerable coverage, few reporters have identified the underlying cause, which is the overwhelmed, antiquated system that allowed it to happen.

There are numerous resources on the web for more information on genetically engineered foods:

Institute for Agriculture and Trade Policy - www.sustain.org/biotech/ Greenpeace USA - www.greenpeaceusa.org/ge/ Union of Concerned Scientists - www.ucsusa.org Ag Biotech Info-Net - www.biotech-info.org

Update by Karen Charman (aurora@ulster.net)

Genetic technologies, like chemical and nuclear technologies before them, have the potential to alter in unforeseen and unwelcome ways all that we depend upon for our survival-our environment, our food, and our health. Like the products of chemical and nuclear technologies, biotechnology products are being ushered out into the environment and onto the market for people to consume without fully considering, let alone understanding, either their long- or short-term impacts.

Through intellectual property patents, biotechnology grants private corporations ownership to previously unowned living things. The economics behind biotechnology are the technology's driving force, but discussion of life patents and their implications are absent from most media accounts and, consequently, public debate.

Scientific understanding of how genes work in organisms is in its infancy. The same is true for scientific understanding of ecology. Yet, without a thorough understanding of the web of life and how its different components interact with each other, it's impossible to know what the true impact of releasing these novel organisms will be or to assess whether we should be taking this genetic gamble.

Much less risky solutions exist to the problems biotech purports to solve.

But they are not being presented in the mainstream media. Instead, most coverage continues to uncritically spread industry-promoted myths about biotechnology while failing to comprehensively and accurately report the technology's impacts, risks associated with biotechnology, and why it is being pushed so hard.

Biotech food has become a flash point with consumers overseas and now that opposition is growing here on the home turf, biotech promoters are attempting to manage the public debate with sophisticated PR. Unfortunately, much of the PR continues to appear in the mainstream media.

A number of citizen groups are now doing excellent work on genetic engineering issues.

The Organic Consumers Association www.purefood.org has a website with a tremendous amount of information and links to other sites covering genetic engineering.

The Institute for Agriculture and Trade Policy www.iatp.org has in- depth information on economics and trade issues related to agricultural biotechnology. The Ag BioTech InfoNet compiles scientific reports and technical analysis on biotechnology and genetic engineering in food production, processing and marketing.

Update by Joel Bleifuss (itt@inthesetimes.com)

The U.S. media has not covered the disturbing public health questions raised by Arpad Pusztai's research into genetically engineered potatoes. Genetic engineering continues to receive a clean bill of health by U.S. regulatory agencies despite the fact that no independent, government-supported research into the effects of genetically engineered foods on mammals has been or is being conducted.

This is in large part because the biotech industry has a sophisticated PR apparatus in place that has so far successfully been able to spin the industry's line that genetically altered food is absolutely safe.

Concerns raised by scientists like Pusztai or Michael Hansen at Consumers Union are all but ignored. As Hansen told me, "But for the folks that criticize it, Pusztai's study is still a much better-designed study than the industry-sponsored feeding studies I have seen in peer-reviewed literature."

Pusztai's are the kinds of experiments that need to be done with engineered foods.

ProjectCensored.org - #7 of the Top 25 Censored Stories of 2000

In These Times January 10, 2000 Title: No Small (Genetic) Potatoes Author: Joel Bleifuss www.inthesetimes.com

Extra! May/June 2000 Title: Genetic Gambling Author: Karen Charman

Multinational Monitor January-February, 2000 Title: Don't Ask, Don't know Author: Ben Lilliston
www.essential.org/monitor/mm2000/mm0001.05.html

Corporate news coverage: Wide coverage in England including The Independent, The Herald, Irish Times, The Guardian, The Times London Washington Post, 10/15/99 p. A-3 (negative review)

The Wall Street Journal attempted to debunk the story with the headline "Attack of the Killer Potato," 2/16/99

Faculty evaluators: Lynn Cominsky, Myrna Goodman, Richard Senghas

Student Researchers: Katie Anderson, Kate Sims, Stephanie Garber,

DR. MERCOLA'S COMMENT:

This is the best review I have read of the original research I had mentioned earlier, regarding the potential implications of eating genetically modified food.

Let me repeat.

Back in 1992 the U.S. Food and Drug Administration had determined that genetically engineered foods were in most cases "the same as or substantially similar to substances commonly found in food" and thus are not required to undergo specific safety tests prior to entering the market.

No Safety Testing Has EVER Been Done on These Foods

With the exception of the study mentioned above which clearly has negative health implications.

It is hard to believe that these companies have been able to manipulate the system for the detriment of all future generations.

Re: THE NIGHTMARE OF TED.

From: Suzanne

T1: sroloff1@home.com

Remote User:

Comments

Hi Kate,

I am sorry your daughter is going through this. I also have graves and TED. I think both had a lot to do with my diet, believe it or not. Things that aggravate TED are: green salads, carrots, smoking, chemicals and preservatives, and for me wheat and soy. This would be an easy thing to have your daughter try and cut out all of these things.

Have her focus on high quality (meaning lean and hormone and antibiotic free) protein at each meal, eggs, very little fruit for now, and vegetables like celery, broccoli, sweet potatoes and squashes, radishes, beets, onions, yams, etc. She can have maybe a salad and serving of carrots a week for now. Definitely if she is a smoker she needs to quit right away. Also good fats like olive oil and flax oil are good poured on her vegetables. Also get rid of yeast and sugar in the diet. Drink lots of water and put cold compresses on her eyes when irritated. The prednisone maybe be helping now, but as soon as she stopped the symptoms will come back and it is a terrible drug with terrible side effects she doesn't need. I would taper off that right away and in the meantime maybe the dietary changes will help.

There is a post further down I made about my graves and ted and what I have done. Mine is almost gone (the ted) and the graves is well under control and numbers are in the normal range. The ted is an autoimmune disease, too, like the graves is. Something is irritating her immune system which could be any number of things including foods.

Look at the supplement suggestions for graves and read all the stories about graves and ted on the main page of this site, you will learn a lot. I was lucky and my ted never got that bad, but it could have, same for the graves. I was

determined to find something before this happened and I did. I found dietary changes and the supplement suggestions on this site along with alot of other research I did.

I know it seems like a nightmare when you are in the midst of these diseases, but you can get better and radiation and/or surgery should be a last possible resort, if any at all. It sounds like she needs to stay on the drugs she is on until things start to stabilize. Both graves and ted can go into remission on there own, too in some cases. They kind of have a life of their own and run their course sometimes. I think nutrition and balancing out ones deficiencies in different minerals is crucial to recovery in both of these diseases.

Copper, magnesium and b complex vitamins are what you usually start with with hyper/graves. Have her try these and see how she feels. Also please have her cut out wheat in all forms (that means anything with white flour in it) for a month and let me know if she is any better.

Suzanne

In an article in today's paper, the incoming president of the American Medical Association took a shot at gun ownership and the impact guns have in the number of fatalities recorded annually in the US.

I wonder if staff provided him with these current statistics?

Number of physicians in the US: 700,000.
Accidental deaths caused by physicians per year: 120,000.
Accidental deaths per physician.... 0.171
(U.S. Dept. of Health & Human Services)

Number of gun owners in the US: 80,000,000.
Number of accidental gun deaths per year (all age groups): 1,500.
Accidental deaths per gun owner: 0.0000188

Statistically, doctors are approximately 9,000 times more dangerous than gun owners.

"FACT: Not everyone has a gun, but everyone has at least one doctor."

Please alert your friends to this alarming threat.
We must ban doctors before this gets out of hand.
As a public health measure, I have withheld the statistics on lawyers for fear that the shock could cause people to seek medical aid.

Antibody testing

From: Christine
T1: mccline@prodigy.net
Remote User:

Comments

Anti-Thyroid Peroxidase antibodies can be elevated in both Graves' and Hashi's.

Best bet for thyroid antibodies:

- TSH Receptor Antibody test
- Thyroid Stimulating Immunoglobulin (Graves' specific)
- Thyroid Blocking Immunoglobulin (Hashi's specific)

There are a couple of others such as thyroglobulin antibodies.

Hope this helps some, Chris

Latest Lab Results: Feedback Desired

From: Ellen Fix
T1: efix@pcdi.com

Remote User:

Comments

Would appreciate anyone's suggestions on TAP dosage/nutritional/supplements based on the following lab results, which to my mind indicate a trend toward Hypo:

TBI (Thyrotropin-Binding Inhibitory Immunoglobulin): 46% (NORMAL: Less than 10%. My results indicate the presence of the Graves antibodies. However, I was told that if you're under 65%, you may have a better chance of going into remission. Over 65% means you should worry.)

T4: 5.5 (NORMAL: 4.5-12.5)

FREE T4: 1.5 (NORMAL: 1.4-3.8)

TSH: 4.29 (NORMAL: .40-5.5)

Re: John and others - hair analysis results - please advise!

From: John

T1: BU007@aol.com

Remote User:

Comments

When selenium is ok on the hair test, then it usually means that the mercury and cadmium levels on the hair test are also accurate. If your selenium were very low, you can't trust the mercury and cadmium results because your body isn't eliminating it (because of low selenium).

Lithium metabolism is a mystery. There is very little research on it. My feeling is that since it is so light, it must have a very short half-life in the body and is therefore probably not a major factor in long-term diseases like thyroid disease. However, it's possible if your daily diet is always low in lithium, it could reduce the rate at which certain minerals like copper enter the cells.

Irregular and thumping heart beat

From: John

T1: BU007@aol.com

Remote User:

Comments

Irregular heart rate and very hard "thumping" heart rate are common to those with thyroid disease. I've gone through many months of this and experimented extensively to determine the nutritional cause. I've tried every available mineral and found that potassium helped sometimes, but not with regularity. What I finally found to be the controlling nutrient was one that I would have never suspected and which none of the nutrition books would indicate: pantothenic acid or vitamin B-5. The Nutrition Almanac says, "Pantothenic acid is widely distributed in foods so a deficiency is rare." In retrospect, this should have tipped me off since this is the "common knowledge" about most of the nutrients involved in thyroid disease." I've found that irregular and pounding heart rate, even when induced by heavy exercise, can be relieved within minutes by taking 250 mgs of pantothenic acid. While taking magnesium and potassium would help somewhat, pantothenic acid would reliably end these heart problems. Once I made sure that I took a little more pantothenic acid each day than B1, B2, B3, and B6, then I've had absolutely no occurrences of irregular or thumping heart beating. What was a chronic and deteriorating situation that lasted for many, many months disappeared in one day. And no other nutrient has that effect. I'm not sure why pantothenic acid has this effect, but I know that it assists copper metabolism and that copper is necessary for proper magnesium and potassium metabolism. At least for hypers, we've seen that low levels of magnesium and potassium are common characteristics of the disease. Copper definitely helps the deficiencies of these alkaline minerals and there are several nutrients that assist copper metabolism. I now consider pantothenic acid as one of the key vitamins that helps copper. Interestingly, until I discovered the powerful influence of pantothenic acid, I needed to take 5-8 mgs of copper a day. Since I began to make sure my B5 intake exceeds the other B vitamins, I no longer seem to need to take copper in that quantity. While the pantothenic acid effect could be just peculiar to me, I think it's worthwhile for anyone with irregular heart rate to experiment with it. Remember that B vitamins are powerful and supplementing in unbalanced amounts can cause, as well as correct, health problems. So if you're taking separate B vitamins, be aware of this and move the supplement amounts back into better balance when the problem is corrected.

For Irena , et al, re Radiation Exposure

From: Min

T1:

Remote User:

Comments

Hi, Irena,

Sorry it took so long for me to dig out this info. It's been an exceptionally busy week.

In the U.S. we use the "rad" as the unit to measure radiation exposure. The SI unit that is used in the entire rest of the world is the Gray (Gy). (I don't know why the U.S. has to be different, but we are.) So if you are from somewhere other than the U.S., you'll have to translate rads to Grays. (1 Gy = 100 rad) The important thing, I think, is that you have something familiar to compare unfamiliar things to.

I-123 thyroid scan and uptake: Total body: 0.0065 to 0.013 rad Thyroid: 2.6 to 5.1 rad

I-131 thyroid ablation: Thyroid: 10,000 rad

CT of head & body: 1.1 rad

Upper GI: 0.245 rad

Lower GI: 0.405 rad

Chest x-ray: 0.005 to 0.020 rad

Lumbar spine x-ray: 0.130 rad

Dental x-ray: 0.010 rad

Round-trip airplane flight from NY to CA & back: 0.005 rad (I've read higher figures for this; I'm giving you the lowest)

Naturally occurring background (ground, air, other people, etc): 0.015 to 0.140 rad/year

Cosmic radiation (outer space, stars, sun, etc): 0.026 to 0.050/year

Natural gas in home: 0.009 rad/year

Building materials: 0.003 rad/year

Drinking water: 0.005 rad/year

Radionuclides in your body (absorbed from food, water & air): 0.039 rad/year

My sources for these data are mostly isu.edu and Oak Ridge Labs.

My editorial comments:

Our DNA has the capability of mending itself if damaged by ionizing radiation, provided it is in small enough doses.

There is a lot of naturally occurring radiation in our environment.

There is probably LESS radiation in our environment than there was eons ago, before long-lived radioactive isotopes decayed away to the degree that they have.

The human race has managed to survive continuous exposure to ionizing radiation.

Medical testing that involves exposure to low-levels of radiation can provide information whose benefits far outweigh whatever dubious risk there might be.

It is important to keep one's radiation exposure to the lowest level reasonably achievable, but without being so irrationally fearful that access to valuable information is missed.

Every patient has a responsibility to himself to be as well-informed about his disease as possible and to take responsibility for making appropriate lifestyle changes to facilitate healing.

Final commentary: I drive 6.1 miles to & from work each day, usually at the height of rush-hour. I recall reading once what the chances were of being in a serious accident, calculated per driving mile in my area. I have been in several minor accidents on my route (THEY hit ME!) but I still get in my car and drive to work 5 days a week, knowing the numbers and having experienced the risks. The alternative would be to be unemployed, hungry, cold and broke, and there are risks to that, too. So I wear my seatbelt, maintain my car well, watch out for the other guy, and hope for the best.

All of which is to say, I wouldn't worry about that thyroid scan if I were you.

Best wishes, Min

Forms of minerals

From: John
T1: BU007@aol.com
Remote User:

Comments

There are many different forms of minerals and you are probably right that the other part of the mineral complex (citrate, aspartate, etc.) has biological functions.

This seems to be a very poorly studied area and the importance of this is not well understood by most people, including myself.

I generally experiment with different forms of minerals to see what works best for me. For example, with calcium/magnesium, I've tried just about every form available and am now using the citrate form because that seems to be very absorbable for me. I can feel the results in minutes.

My general feeling is that the rest of the molecule isn't as important as the mineral and that the important thing is to find the form that accomplishes your nutritional requirement, which often means experimentation.

I would agree that your rapid rise in TSH is unusual. Perhaps this means that your pituitary is functioning very well and that is not the case in individuals where the TSH stays low for a long time. It would be interesting to see if your selenium is higher than most since some research indicates that selenium is somehow involved in TSH recovery.

Re: More Levo doesn't Help

From: John
T1: BU007@aol.com
Remote User:

Comments

Hi Bob,

It's very interesting that increasing the replacement thyroid hormone doesn't help your symptoms. I think this is good evidence that your symptoms are the result of iron-deficiency anemia as your hair analysis indicates.

Lack of iron will prevent the red blood cells from getting adequate oxygen to your cells. The decreased rate of cellular respiration will result in low energy and poor heat production which is exactly what your experiencing.

As an analogy, if an anemic person were to consume six cups of coffee each day, this will not correct the anemia or have much effect in increasing energy. Thyroid hormone is very similar. It cannot increase the delivery of oxygen to the cells other than the minor role it has in increasing the heart rate.

In hyperthyroidism we see a similar phenomenon. The person is copper deficient so there isn't enough hemoglobin to carry oxygen. The increase in thyroid hormone increases the heart rate, but the blood is so deficient in oxygen that the person suffers from very low energy and can hardly move or think. The only difference is that in hyperT there is excess iron which is available to produce the hormone norepinephrine which is one of the body's prime heat-producing hormones.

Low body temperature is a very important nutritional clue. It means iron deficiency. However, it could be from lack of iron, folic acid, B-12, manganese, the other B vitamins or a combination. That's where the experimentation comes in.

Re: chocolat

From: John
T1: BU007@aol.com
Remote User:

Comments

Hi CD,

Chocolate is high in copper and magnesium which are two minerals that are deficient in hyperthyroidism.

Itching of the palms and bottoms of the feet is a symptom of B5 (pantothenic acid) deficiency. B5 also is important for copper metabolism. You may want to try B5 to see if it relieves your itching. John

Maca

From: Ann
T1: lowell.barron@sympatico.ca
Remote User:

Comments

Hi, Has anyone used Maca. Look it up on the internet. Interesting. It was recommended to me by a pharmacist who specializes in natural remedies. He is a licensed pharmacist and a Master herbalist. He says that it is an adaptogen - meaning that it moderates function either way. I took it for awhile but was also taking other thyroid stimulating substances such as l-tyrosine (which is a pre-cursor to thyroxine), Fucus vesiculosus, and potassium iodide. Well, for any of you that have read my earlier posts, I triggered a hyperT state and had to back off all for awhile and am just experimenting again.

Maca is suppose to increase libido and I find that any thyroid stimulation does that.

Re CLA - I did try that awhile back but would like to try again not that I am off chocolate and other things and observe the thyroid connection. FYI John - my naturopath is very keen on the many benefits of CLA. Ann

fluoride, hypothyroid

From: beth
T1:
Remote User:

Comments

Here's an excerpt from an article linking fluoride consumption with hypothyroidism. The complete article also mentions cadmium.

"Schuld then asked Woodruff to read from the actual data of the study. It showed an increase of 18% in observed thyroid cancers in the fluoridated areas when compared to non-fluoridated areas. "No association?", Schuld asked, and then proceeded to read from newspaper articles from China, where entire villages are being re-located due to fluoride contamination and where fluoride is being openly acknowledged as the cause of thyroid cancer, Kaschin-Beck disease and iodine deficiency.

Next Schuld presented a paper which had investigated whether fluoridation had a protective effect on slipped epiphysis, one of the most-common hip disorders observed in older children and adolescents. Schuld said that this paper was especially close to his heart as the condition has been strongly linked to hypothyroidism since the 1920s. Schuld added that this was acknowledged by the study authors themselves who had provided more than 16 references in the paper's first paragraph. The York team which had been informed of fluoride's effects on thyroid hormones should have woken up here, Schuld said.

Schuld then read excerpts from the York Report which had found "the direction of association to be positive (a protective effect) in girls and negative (increased risk) in boys", but that neither of these was statistically significant.

Schuld again asked Woodruff to look at the actual data in the paper. Woodruff saw an 18 per cent increase of the disease in males in fluoridated areas.

"Would you consider an 18% increase here significant?" Schuld asked Woodruff, who at this time joined Schuld in declaring the Review a total scientific fraud and called it an example of severe and gross scientific misconduct. Schuld then read further excerpts from the paper in question, citing how the authors of the study had found that more cases had come from rural areas, and "that, in general, the rural areas had higher fluoride levels than suburban or urban regions".

"In other words, the higher the fluoride levels, the more slipped epiphysis", said Schuld, "another obvious sign showing the anti-thyroid activity of fluoride".

Schuld ridiculed the claim by York that fluoridation showed protective effects in girls. "It is known that the disease almost NEVER occurs in girls once menses have begun, so walking around with a toilet bowl on your head would show so-called protective effects in this group", exclaimed Schuld

Schuld emphasized the issue of delayed eruption of teeth, explaining how it has been established since the 1930s that thyroid hormones control tooth eruption. "

<http://www.rense.com/general4/flu.htm>

Re: Endocrinologist?

From: Joan
T1:
Remote User:

Comments

Kathy, I found calcium and magnesium helped my heart rate. Co-enzyme Q is also good for the heart and gets depleted with the hyper-t heart. I found the calcium helped a lot with my fatigue and I also try to correct my poor sleeping habits. I used to flip flop hyper-hypo. Joan

Re: Leg Cramps

From: Darlene
T1: Dittomom1@aol.com
Remote User:

Comments

I had them too. Legs were quite weak, too. Tried the cal/mag etc. to no avail. Then one day on a lark, I took an amino acid complex twice a day. These were huge ones, made from milk. Cramping and weakness were G O N E in two or three days, never to return.

Re: Leg Cramps

From: John
T1: BU007@aol.com
Remote User:

Comments

Hi Deanna,

Nutrition is complex and all nutrients work with other nutrients. Magnesium does relieve leg cramps, but only if all the other nutrients that help magnesium are present.

Copper is one of the main nutrients that helps magnesium relax the muscles, but I imagine that you are taking copper. Also it seems that extended use of magnesium can deplete potassium and potassium seems to be necessary for magnesium to work correctly. It's possible you need more potassium.

The B complex vitamins seem to be involved in just about every metabolic process. If a deficiency of one or more of the B vitamins exists, it's possible that copper may not be able to help magnesium or some other pathway may not work.

Pantothenic acid (B5) seems to help the copper/magnesium metabolism and will reduce the heart rate and cramping situation. You might want to experiment with 250 mgs of B5 to see if that helps. If that doesn't work, you might try biotin, or some of the other B vitamins, or just take a B complex 50 or 100.

Another vitamin deficiency associated with cramps is vitamin E. Vitamin E also seems to have thyroid effects since it works with selenium and iron and also increases estrogen production which is a hormone that can slow the thyroid under most circumstances.

Let me know if any of these suggestions help. If none of them help at all we'll have to dig deeper. John

Re: Leg Cramps

From: Joan

T1:
Remote User:

Comments

Deanne, A Potasium deficiency can cause leg cramps. You may also need a source of vitamin D to help the cal/mag supplements. I use cod liver oil for the vit D and bananas or potassium pill supplement. You might want to watch your sodium salt intake and drink lots of water too. Joan

Selenium Content in Foods

From: Christine
T1: mccline@prodigy.net
Remote User:

Comments

I'm not sure how accurate these figures are. It's from my older Nutrition Almanac - 2nd edition, 1984:

Approximate SELENIUM content in some foods://///

1 cup grape juice - 10 mcg (not sure if purple or white) ///

1 cup orange juice - 14.9 mcg ///

1 banana - 1.5 mcg ///

1 pear - 1.2 mcg ///

1/2 chick breast - 19.2 mcg ///

1 chicken drumstick - 13.3 mcg ///

4 lg clams - 55 mcg ///

4 oz lobster - 118 mcg ///

4 oz oysters - 55 mcg ///

4 0z scallops - 87 mcg ///

4 oz shrimp - 226 mcg ///

4 oz cod - 46 mcg ///

1 c mushrooms - 8.54 mcg (not sure which kinds) ///

10 radishes - 2 mcg ///

4 oz almonds - 1.4 mcg ///

4 oz brazil nuts - 72 mcg (seems pretty high - wonder if misprinted?) ///

4 oz hazelnuts - 1.35 mcg ///

4 oz pecans - 1.62 mcg ///

1 slice whole wheat bread - 15.5 mcg ///

1/2 c wheat bran - 18 mcg (the grain, not the cereal) ///

1/2 c uncooked brown rice - 36 mcg ///

1 c creamed cottage cheese - 11.3 mcg ///

1 oz swiss cheese - 2.83 mcg ///

1 oz processed American cheese - 2.52 mcg ///

1 c whole milk - 3.17 mcg ///

1 whole egg - 3.3 mcg ///

1 egg white - 1.88 mcg ///

1 egg yolk - 2.96 mcg ///

1 Tbs light molasses - 5.2 mcg (no info on blackstrap) ///

1 Tbs vinegar - 13.3 mcg (not sure which kind) ///

Best Wishes, Chris

Copper Content in Foods

From: Christine
T1: mccline@prodigy.net
Remote User:

Comments

Hi Lisianthus -

I understand the frustration about supplements. In fact, I'm unable to tolerate the supplements myself, and have done well with food sources. I started off with replenishing my copper and selenium reserves (selenium content listed in next post).

Here's a list of some copper-containing foods. You can find a great food content table in the Nutrition Almanac, which lists most nutrients -

(If this all runs together, I apologize - have tried to separate the listings with /// just in case):

COPPER CONTENT IN FOOD - (In Milligrams)/////

1 oz baking chocolate (unsweetened, dark) - .748 mg ///

1 Tbsp molasses, blackstrap - .284 mg ///

1 Cup whole milk - .50 mg ///

1 avocado - .527 mg ///

10 dried figs - .585 mg ///

1 Cup raisins - .498 mg ///

1/4 lb beef liver - 3.2mg ///

1/4 lb lamb liver - 6.2 mg ///

1/4 lb veal liver - 9.0 mg ///

1 duck liver - 2.62 mg ///

1 goose liver - 7.07 mg ///

1 turkey liver - .512 mg ///

NUTS -/////

1/2 Cup almonds - .59 mg ///

1/2 Cup Brazil nuts - 1.07 mg ///

1/2 Cup cashews - 1.41 mg ///

1/2 Cup hazelnuts - .86 mg ///

1/2 Cup peanuts - .31 mg ///

1/2 Cup pecans - .57 mg ///

1/2 Cup shelled pistachios - .76 mg ///

1/2 Cup pine nuts - 1.16 mg ///

1/2 Cup pumpkin or squash seeds - .95 mg ///

1/2 Cup sesame seeds - 1.2 mg ///

1/2 Cup sunflower seeds -1.29 mg ///

1/2 Cup walnuts - .70 mg ///

2 Tbsp tahini (sesame seed butter) - .48 mg ///

FISH -/////

1/4 lb cod - .57 mg ///

1/4 lb haddock - .26 mg ///

1/4 lb herring - .34 mg ///

1/4 lb salmon - .22 mg ///

1/4 lb trout - .37 mg ///

1/2 Cup tuna - .10 mg ///

SHELLFISH -/////

1/4 lb crab - 1.47 mg ///

1/4 lb lobster - 2.49 mg ///

1/4 lb oysters - 1.36 mg ///

1/4 lb scallops - .14 mg ///

1/4 lb shrimp - .49 mg ///

3.5 oz snails - .40 mg ///

VEGETABLES and BEANS -/////

1 Cup asparagus - .20 mg ///

1 Cup collard greens - .484 mg ///

1 Cup cooked kidney beans .647 mg ///

1 Cup cooked lentils - .54 mg ///

1 Cup cooked lima beans - .519 mg ///

1 Cup okra - .94 mg ///

1 Cup parsley - .293 mg ///

1 Cup green peas - .257 mg ///

1 Cup cooked split peas - .50 mg ///

3 medium pimientos - .60 mg ///

1 Cup potato - .388 mg ///

1 lg baking potato - flesh and skin - .26 mg ///

1 Cup pumpkin - .33 mg ///

1 Cup soybean sprouts - .30 mg ///

1 Cup spinach - .32 mg ///

1 sweet potato - .22 mg ///

1 Cup tomato juice - .246 mg ///

1 Cup yams - .484 mg ///

Hope this helps - Selenium content to follow,

Best Wishes, Chris

Simple Exercise to help regulate thyroid function

From: Cathy

T1:

Remote User:

Comments

Hi, I wanted to share with you all an exercise which, according to The Encyclopedia of Natural Healing, will help to regulate thyroid function. It is extremely easy to implement in the comfort of your own homes. "Water Stepping- Step bare legged into water until just below the knee. Use a large bucket, or bathtub for this purpose. Walk back and forth, always lifting one leg out of the water. Walk like a stork, lifting each leg completely out of the water. The change between the cold water and the warm air will produce a healing effect. Ten to fifteen seconds of stepping might be all you need. Stay in the water only as long as you remain comfortable. Immediately, wipe off the water, dry, put on socks and warm up the feet by walking about." This technique was developed by a Father Sebastian Kneipp and is offered at many spas and clinics in Europe.

Re: For Jules - Elaine's website

From: Christine

T1: tnccline@prodigy.net

Remote User:

Comments

Hi Jules -

I tried to email you privately, but I got a reply from a guy who was confused about what I had written. Now I see why people look at us like we're from outer space when we try to explain this disease.....

I did not post the info because of its length, but will just go ahead and post it here.

Chris

You have a stimulating TSH receptor antibody test there. I'm a little confused because my endo, in Los Angeles, runs a TRAb (TSH receptor test) and a TSI (Thyroid Stimulating Immunoglobulin) as 2 separate tests.

My TSI a year ago was within the normal range. The TRAb was just slightly elevated.

My endo ran these same 2 tests last week and I expect a call from him soon with the results. Will let you know if there was a change.

Last year I tried for remission but dropped the Tap too fast. I Went from 15 mg a day for 3 weeks, then 10 for 3 weeks, then 5. I ended up in the hospital with atrial fibrillation. My Total T-4 was 21 (range: 4.5 to 12). I went back on 15 mg a day of the Tap.

But this time I split it into 3 times a day. Then I lowered very slowly - this cockeyed way with splitting the pills, but still taking an equal amount 3 times a day.

A couple of months after the failed attempt last June, I also started eliminating gluten, most sugar, adding acidophilus, and adding more protein.

Don't know exactly which worked. Maybe both slowly lowering the pills and eliminating gluten? I know the IBS (Irritable Bowel Syndrome) and stomach probs aren't nearly what they used to be and the thyroid is healing.

Where do you purchase your Tapazole? They call them pharmacies here. Are they called "chemists" there? Ask one of them what the best way to split a 5 mg pill would be.

I just take a saucer and hold the 5 mg pill over it. I break the pill in half. If there is a smaller half, I consider that 2 mg. I break that in half to get one mg.

If they break evenly, then pinch a bit off of each - making each a 2 mg pill. Do this with the bigger half when they break unevenly.

Some may crumble into dust, but many of them make it. Soon you'll be able to recognize the correct size of the piece of pill in the palm of your hand.

Will dig out my old antibody tests. Is difficult to get these tests here. Will write more soon.

Best Wishes, Chris

Re: Replies to Larry and Christine from 5/30 post

From: Christine
T1: tnccline@prodigy.net
Remote User:

Comments

Hi Cressy -

Glad we could help. You're lucky to find an endo who will prescribe the Tap and is willing to work with you. Make sure you can get your thyroid levels checked every 3 weeks or so, and sooner if you feel bad.

Arrange to obtain your results as soon as possible, to avoid the "lab results shuffle" - You need to know the levels when you're tested, not 2 weeks later. A few of us in this group have been jacked around over our results lately.

T-4 testing takes a few hours, and T-3 testing takes a couple of days, depending on whether they have to send the test out. The T-3 is very important, too. Your T-4 can be very low, and the T-3 can be climbing right on up.

We find that if you continue to call the doctor's office every hour you will get someone to finally spill the test results to you. Sheesh!!

I find it interesting, but not surprising, that your endo says a connection between gluten intolerance (celiac symptoms) and thyroid disease is uncommon. Wonder where he gets this information. I've had thyroid disease for years and I've had moderate to severe digestive problems for years, also. I've cleared up the gut and balanced my system, and my thyroid is healing. And it seems that most people who post here are the same way. Doctors should open their minds.

We should conduct a survey on this item. Many of us are finding there is a definite connection between the gut and the thyroid disorders. In fact, it appears to be the rule rather than the exception. An impaired digestive system will not absorb nutrients correctly.

And DON'T think the gut ISN'T affected by stress, both emotional stress AND physical stress, such as pain.

You can have many symptoms with Graves' hyperthyroidism. When I was first diagnosed as severely hyperthyroid in 1979, I had gained 50 pounds in the previous 5 months. I have annoying joint pain when I'm hyper also. Increased appetite is a sure-fire hyper symptom.

Going wheat-free, gluten-free, yeast-free, adding acidophilus, cutting way back on the sugar, increasing your protein intake, and trying to relax is a really good start. Study the supplement list and start balancing your nutrients. Study "nutrients and toxics" and start eliminating the "poisons." You will find the balance that is right for you, but it takes stick-to-it-ive-ness!

It's not surprising that your microsomal count is normal. This is supposed to indicate Hashimoto's hypothyroidism if positive. However, I'm supposed to have Graves' but my microsomal or peroxidase antibody levels are always above normal. Go figure.

The antibody test for Graves' is the Thyroid Stimulating Immunoglobulin (TSI) and the TSH Receptor Antibody (TRAb).

If I left something out (as if this isn't long enough!) please ask again. Good to hear from you!

Best Wishes, Chris

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ASTHMA

From the Nutrition Almanac: (contributed by Penny)

NUTRIENTS THAT MAY BE BENEFICIAL IN TREATMENT OF ASTHMA

Vitamin A 15,000 IU daily

Beta-carotene 15,000 IU daily

Vitamin B complex 50 mg 4/daily

Vitamin B6 50 mg 3/daily

Vitamin B12 100 mg 2/daily between meals

Choline

Inositol

Panthenic acid 50 mg 3/daily

Vitamin C and bioflavonoids 1500 mg 3/daily

Vitamin D 600-14,000 IU daily

Vitamin E 600 IU and up

Unsaturated fatty acids

Selenium 200 mcg daily

Bee pollen up to 1 tsp daily

Calcium

Manganese 5 mg 2/daily for 10 weeks

Magnesium 750 mg daily

Coenzyme Q10 100 mg daily

kelp 10/daily for 21 days, then 3/daily

Quercetin C 500 mg 3/daily

Cromolynsodium

Bromelin 100 mg 3/daily

L-methionine 500 mg 2/daily

Here's a summary of some of the text:

Meat, eggs, and dairy products can trigger allergens. Nuts, chocolate, colas, milk and MSG are also triggers. Metabisulfate (a food preservative), dust mites, roaches, cats and dogs can all bring on an attack. Exercise, viral infections and sinusitis are also triggers.

Emphasis is placed on Vitamins A, E, B complex, B6, B12 and C. Magnesium deficiency may play a role in the cause of asthma. Fish oils may help. Avoid oils high in omega 6 fatty acids (safflower & sunflower). A mix with flax oil is a good idea. Helpful foods may be, onions, garlic, fruits and vegetables high in C. Vegetarian diets benefit those with Asthma. Hot foods like chili pepper 3xweek may help breathing. Caffeine in coffee can dilate bronchial tubes during an attack. A high fluid intake and inhalation of steam may help liquefy mucus and make it easier to be expelled from the air passages. Avoid smoking or smokers.

Herbs that are helpful are chickweed, echinacea, propolis, horsetail, pau d'arco tea, nettle (may have side effects), juniper berries, damiana tea to calm nerves, licorice root, bark tablets, slippery elm, ephedra to dilate bronchioles (tolerance levels rise with use) and forskolin to dilate the bronchioles and prevent inflammation (but effects are brief and may cause cardiovascular problems). Thai ginger has same positive aspects. Snakeweed or euphorbia (expectorant but may be toxic to kidneys). Ginkgo is good for all lung diseases, (ginkgolide B is being studied for asthma), lobelia aids during an attack, red clover is an expectorant, and schizandra is a chinese herb (an astringent). Oil of eucalyptus and sandalwood massaged into back and chest is helpful. Frankincense is also good. A great deal

of mucus requires myrrh. Homeopathic remedies include, antimonium tartaricum 6c, Bryonia 6c, Drosera 6c, Spongia 6c and Corallium rubrum 6c for coughing discomfort. Exercise can be beneficial. Tennis or swimming may be best because they take place in warm, humid areas and use short bursts of energy. Pretreatment with an inhaler and a warmup and cooldown period are essential.

From Dr. Mercola's site at www.mercola.com:

IV Magnesium Helps Children with Moderate to Severe Asthma

Intravenous magnesium therapy may provide **"remarkable"** benefit to children with moderate to severe asthma, according to a new double-blind placebo-controlled study.

Researchers administered a single dose of magnesium sulfate or a placebo (saline solution) to 30 children experiencing moderate to severe exacerbations in their asthma.

The children ranged in age from 6 to 18 years old.

Immediately following the infusion, the magnesium group had a significantly greater percentage of absolute improvement from baseline in each of the following parameters:

- Predicted peak expiratory flow rate (8.6% vs 0.3%)
- Forced expiratory volume in 1 second (7.0% vs 0.2%)
- Forced vital capacity (7.3% vs -0.7%)

The improvement was greater at 110 minutes:

- Peak expiratory flow rate (25.8% vs 1.9%)
- Forced expiratory volume in 1 second (24.1% vs 2.3%)
- Forced vital capacity (27.3% vs 2.6%)

In addition, **50% of the patients who received intravenous magnesium were discharged to their homes versus none of those who received the placebo.**

Researchers conclude that, "Children treated with 40 mg/kg of intravenous magnesium sulfate for moderate to severe asthma showed **remarkable improvement in short-term pulmonary function.**"

Archives of Pediatrics and Adolescent Medicine October 2000;154:979-983

Polyunsaturated Fats Contribute to Asthma

Breastfeeding Found to be Protective Also

Toddlers who consume large amounts of margarine and foods fried in vegetable oil may be **twice as likely** to develop asthma as their peers who eat less of these foods.

Diets high in polyunsaturated fat--found in margarine, vegetable and sunflower oils--boost levels of omega-6 fatty acids in relation to levels of omega-3 fatty acids. Omega-6 fatty acids contribute to the production of compounds involved in inflammation and may therefore contribute to inflammation of the airways. Omega-3 fatty acids--found in fish inhibit inflammation.

The investigators also found that children who were breast-fed in the first weeks of life had a **lower asthma risk**. They note that previous studies have also linked breast-feeding with lower asthma risk, possibly because breast milk provides immune factors not present in formula.

The authors estimate that a high intake of polyunsaturated fat accounts for **17%** of asthma cases in the study, and not breast-feeding can be blamed for **16%** of cases.

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AUTISM

The following is an article from Dr. Mercola's site, www.mercola.com, about the connection between mercury toxicity and autism. It basically states that the symptoms of autism are identical to the symptoms of mercury toxicity and that mercury toxicity is most likely the cause of autism. Infant get mercury toxicity from vaccinations because of the mercury-containing compound thimerosal. Thimerosal used to be used as a preservative in contact lens solution and may be in many other substances. Look at all products for thimerosal and any chemical with "mer" in it. This "mer" may indicate that it is a mercury compound. If you have children you don't want them to receive any vaccination with mercury in it.

Most likely mercury toxicity is involved in thyroid disease also, so as you read this article keep in mind that later in life this mercury load in the body can manifest as hypothyroidism or hyperthyroidism. Also remember that the best antidote to mercury toxicity is selenium.

Autism and Mercury

by Tim O'Shea, DC

This article is excerpted from Dr. O'Shea's forthcoming revised edition of The Sanctity of Human Blood.

Inquiry into vaccine safety is exploding like never before, even in the popular press. Research coming from dozens of mainstream medical studies can no longer be easily suppressed, as it has been in the past, especially with the prevalence of online information exchange.

Last September, some 2,000 people, mostly MDs, assembled at the Town and Country resort in San Diego to hear the latest research on autism. Following the April 2000 Congressional hearings on autism and vaccines, this epidemic can no longer be ignored.

The figure of one autistic infant for every 150 is now widely documented.

Dr. Stephanie Cave presented enlightening data on mercury toxicity, drawn largely from the brilliant work of Sallie Bernard. Dr. Cave explained how:

By age two, American children have received 237 micrograms of mercury through vaccines alone, which far exceeds current EPA "safe" levels of .1 mcg/kg. per day. That's one-tenth of a microgram, not one microgram.

Three days in particular may be singled out as spectacularly toxic for infants:

Day of birth: hepatitis B-12 mcg mercury

30 x safe level

At 4 months: DTaP and HiB on same day - 50 mcg mercury

60 x safe level

At 6 months: Hep B, Polio - 62.5 mcg mercury

78 x safe level

At 15 months the child receives another 50 mcg

41 x safe level

These figures are calculated for an infant's average weight in kilograms for each age.

These one-day blasts of mercury are called "bolus doses". Although they far exceed "safe" levels, there has never been any research conducted on the toxicity of such bolus doses of mercury given to infants all these years.

Inconceivable

Historically, the toxicity of mercury has been known for more than a century. The Mad

Hatter was more than a fantasy character from Alice in Wonderland. Mad Hatter's disease became well known in England in the mid-1800s, when hat-makers were subject to inhaling the vapors from the mercury-based stiffening compound they used on felt to make top hats.

Sources of Mercury

It is interesting to learn that common household remedies that were used up into the 1960s like mercurchrome and "teething powder" were often the cause of acute mercury poisoning and disease.

In the U.S., EPA mercury toxicity studies have involved contamination from fish, air, and other environmental sources. This is inorganic mercury (methylmercury).

Methylmercury has long been associated with serious neurological disorders, demyelinating diseases, gut disease, and visual damage.

The mercury in vaccines, however, is in the form of thimerosal, which is 50 times more toxic than plain old mercury (methylmercury).

Reasons for this include:

- **Injected mercury is far more toxic than ingested mercury.**
- **There's no blood-brain barrier in infants.**
- **Mercury accumulates in brain cells and nerves.**
- **Infants don't produce bile, which is necessary to excrete mercury.**

Thimerosal is organic mercury

Once it is in nerve tissue, converted irreversibly to its inorganic form.

Thimerosal is a much more toxic form of mercury than one would get from eating open-sea fish; it has to do with the difficulty of clearing thimerosal from the blood.

Thimerosal is converted to ethylmercury, an organic form that has a preference for nerve cells.

Without a complete blood-brain barrier, an infant's brain and spinal cord are sitting ducks. Once in the nerve cells, mercury is changed back to the inorganic form and becomes tightly bound. Mercury can then remain for years, like a time-release capsule, causing permanent degeneration and death of brain cells.

Bernard also notes that the body normally clears mercury by fixing it to bile, but before six months of age, infants don't produce bile. Result: **mercury can't be excreted.**

Four separate government agencies have set safe levels for methylmercury, but no safe levels have ever been set for thimerosal, because thimerosal isn't included in toxicity studies.

Theoretically, that means that the above excesses of safe levels of mercury on the single days listed above are actually 50 times higher.

Does the fact that the mercury is accompanied by a vaccine somehow place it above scrutiny? The Sallie Bernard study of vaccines and mercury toxicity was probably the main reason Congress began to see the obvious correlation.

Mercury And Vaccines

Here's a curious "coincidence." In the late 1930s, Leo Kanner identified autism as a new type of mental disorder. So when was thimerosal introduced into vaccines?

The 1930s

A few years ago, Bernard and her associates began to notice a striking similarity between the symptoms of autism and the symptoms of mercury poisoning. The more research she did, the more it seemed that these two diseases were virtually identical.

Autism and mercury poisoning damage the: brain/nerve cells; eyes; immune system; gastrointestinal system; muscle control; and the speech center.

Although mercury toxicity has been studied for decades, and EPA safety levels have been set, during all that time a child's greatest exposure to mercury - thimerosal in vaccines - was never even included in the toxicity studies!

The talk has always been about methylmercury from seafood and the environment, totally ignoring the two most toxic sources of mercury for children: vaccines and dental amalgams.

The EPA has no jurisdiction over drugs.

That's the FDA's job. This is why vaccines and amalgams don't even figure into the equation when it comes to setting "safe" levels of mercury.

But the FDA does have jurisdiction over drugs and drug companies, right? And over drug company publications, like the Merck Manual, the standard cookbook for drugs and diseases found in every doctor's office in the world.

Surely the FDA, as the government agency charged with safeguarding the nation's health, would want the section on mercury toxicity to warn doctors about the two biggest sources for children: thimerosal and dental amalgams, wouldn't you think?

Yet looking at the Merck Manual (1999), in the section on mercury poisoning (p. 2636), thimerosal and dental amalgams again are not even mentioned!

How can this be, when mercury is widely acknowledged as the third most deadly toxin in the world and thimerosal and amalgams dwarf the trace amounts of mercury from fish and other environmental sources of mercury?

Only one thing can a blackout information over an entire area of study for years at a time in this way - **big money.**

Such an omission probably wouldn't have anything to do with the revolving door that exists between the FDA; the EPA; the NIH;

"and the sweet positions held by their members before and after those grueling years of public service; or with the 800 waivers of the conflict of interest rule that the FDA has granted in the past two years to "experts," who are paid consultants to the drug companies-consultants who are also members of the FDA advisory committees that make decisions about whether or not to approve vaccines and drugs..." (USA Today, Sept. 25, 2000)

No, of course not.

Soaking up the Mercury

In the San Diego conference on autism, Dr. Amy Holmes gave perhaps the only lucid presentation about treatment. She explained how chelating drugs alone, which go through the blood like Pac Man munching up mercury, don't do much good for autism.

That's because most mercury clears from the blood very soon. Mercury in thimerosal is stored in the gut, liver and brain, and as previously mentioned, becomes very tightly bound to the cells. Once inside those cells, or inside the blood-brain barrier, the mercury is reconverted back to its inorganic form.

Locked into these cells, the mercury can then do either immediate cell damage or become latent and cause the onset of autism, brain disorders, or digestive chaos years later.

Dr. Holmes reported success using alpha-lipoic acid as an agent to cross the blood-brain barrier to soak up mercury. Once the mercury is brought back into the bloodstream, standard chelators like DMSA can then take it out.

Dr. Holmes has used her protocol on about 300 autistics so far, and shows consistent increases in IQ scores.

FDA: Protector of Whom?

In the face of all this new awareness, it was astounding that in July 2000 the FDA came out with the "parallel-universe" pronouncement that "vaccines have safe levels of mercury."

Especially after their 1998 position:

"... over-the-counter drug products containing thimerosal and other mercury forms are not generally recognized as safe and effective."

As if there were any doubt as to who's really running the show, inconceivable also is the impotence of FDA's request to the vaccine manufacturers to discontinue the use of thimerosal in vaccines ([LINK TO ARTICLE ON SITE](#)) The same month that MMWR published this, the CDC made the same milquetoast request.

It's a bit like saying: "Hey guys, since all these kids are turning into vegetables and most of our researchers know it's the mercury, would you mind not putting any more thimerosal in your vaccines, please?"

No hurry, though. Whenever you're ready. No need to dump all those batches of vaccine just because people are finding out it's the mercury that's destroying children's brain cells."

The members of the FDA who decide which vaccines get approved make up the advisory board. In his recent House investigation on vaccines, Rep. Dan Burton found out that financial statements of advisory board members are "incomplete."

Noting that this is the only branch of government that allows incomplete financials, in September 2000, Burton called the advisory board's sweetheart arrangements with the vaccine manufacturers a "violation of the public trust."

This includes 70 percent of advisory board members owning stock in vaccines, owning patents on vaccines, and accepting salaries and benefits as employees of the drug companies.

A Matter of Trust

Still think you can trust the government or your physician with your children's blood? Despite the facts and events cited above, consider this joint statement of the U.S. Public Health Services and the American Academy of Pediatrics:

"There is a significant safety margin incorporated into all the acceptable mercury exposure limits. There are no data or evidence of any harm caused by the level of exposure that some children may have encountered in following the existing immunization schedule ... Infants and children who have received thimerosal-containing vaccines do not need to be tested for mercury exposure" ([TRY TO REPLACE THIS WITH LINK FROM SITE MMWR, vol. 45, 1999](#)).

These are blatant Orwellian distortions. No harm?

- **What about the autism epidemic and all the evidence linking it with mercury cited above?**
- **What about the single day doses of mercury cited above that are dozens of times in excess of the EPA's own safety levels?**
- **If everything is so safe, then why did they ask the vaccine pushers to kindly discontinue thimerosal from vaccines as soon as possible at the end of this same statement?**

It is beyond the scope of this paper to really go into the politics of mercury. In researching mercury toxicity, a whole area of "dry rot" has been unearthed that deserves its own story. This is the shocking story of how the American Dental Association and the California Dental Association have been systematically hiding the truth about mercury toxicity in fillings for decades.

Silver fillings aren't just silver. They're 50 percent mercury and extremely toxic; every dentist knows it (www.altcorp.com, <http://www.amalgam.org/>).

In a ludicrous blast of irony, both the ADA and the CDA have inserted into their "code of ethics" strict commandments forbidding dentists from ever revealing to patients the realities of mercury toxicity.

No dentist is allowed to recommend removal of mercury amalgams for health reasons, nor may tell the patient about mercury toxicity even if the patient asks. This gag order has been in place for since the beginning of American dentistry. Exaggeration? Check their websites out:

www.amalgam.org/#anchor69176 www.amalgam.org/#anchor69541

Do you think dentists put mercury into their own families' teeth? Ask them. Anyone who is not a dentist is not constrained by the gag order, imposed on American dentists by the ADA, against telling patients what many perceptive researchers in the field of mercury toxicity already know: that no children should ever get mercury amalgam fillings.

Laughingstock of the West

Researchers across Europe are generally appalled at the massive amounts of vaccines given to American children under two years old. Although Europeans are not as obsessed with vaccines as we are, they do vaccinate.

But most of Europe gives very few vaccinations to children under two years old, primarily because of the unformed gut, immune system, and blood-brain barrier.

This intellectual isolation of ours regarding vaccines is a testimony to the suffocating "brain control" exerted on us by the popular press and all media. Like sheep to the slaughter, we don't know enough to be appalled by our own ignorance.

Autistic Gut

Headlining the September 2000 San Diego Conference was Andrew Wakefield, the British surgeon whose shocking new discoveries show that mercury toxicity alone is not the only factor linking vaccines with the autism epidemic. Dr. Wakefield's research centers around the MMR vaccine - measles/mumps/rubella - which does not contain thimerosal.

Expanding on his presentation at the April 2000 Burton hearings, Dr. Wakefield explained how at least three-quarters of autistics have pathologically blocked bowels, due to the huge swelling of the tissue lining the intestine.

In virtually every autistic patient they examined, this nodular hyperplasia is both an immune response and an autoimmune response that Wakefield and O'Leary have clearly linked to the presence of measles virus from the MMR shot. No other virus was found in those cells.

It is a new bowel pathology.

Wakefield showed graphs of the U.S. and U.K. 10 years apart that were identical in tracing the skyrocketing incidence of autism just after the MMR vaccine was introduced.

He also showed how the incidence of measles had dropped over 85 percent on its own before the MMR was introduced.

One incredible study cited by Wakefield showed how 76 percent of children whose mothers were exposed to atypical measles became autistic after the MMR shot! He called this a "background susceptibility" or predisposition to autism.

Wakefield reminds us that in neither country have there ever been comparative studies on giving multiple vaccines (polyvalent) on the same day.

This custom of ours, with both the DPT and the MMR, is not scientific by any stretch, and is primarily for the convenience of those administering the shots, and those being paid per vaccine. As a result, there is a good chance of geometric ill effects.

Then Wakefield cited the original MMR study (Buynak, Journal of the American Medical Association 1969, vol. 207).

Not only was the safety of multiple vaccines never mentioned, there was no follow-up to the study to see if their conclusions were correct.

In the usual manner of testing vaccines on the live population, MMR was simply tacked onto the mandatory schedule, and we've never looked back.

Despite studies in 1981 on Air Force personnel showing major synergistic adverse effects in the gut from the combination of measles and rubella vaccines, the mandatory schedule went unchanged.

A Glimmer of Hope

Despite these formidable obstacles, doubts are creeping into the overall public "consciousness" about the safety of vaccines. At one in 150, the fact of autism as an epidemic can no longer be covered up.

The work of Wakefield, O'Leary, Megson and Bernard is getting more and more difficult to explain away. Rep. Dan Burton seems relentless in his efforts to acquaint Congress with the meretricious relationship between the FDA Advisory Committee and the vaccine manufacturers.

The massive advertising campaign about the safety of vaccines in the popular media, which is certain to be stepped up in the next few months, is going to look very hollow in the light of clean, unbiased research that is not funded by parties who stand to make billions from certain predetermined results.

And the internet makes this well-referenced, scientific work accessible to the public without the usual monodimensional smokescreen from the popular press.

Ultimately, the value of the San Diego "Conference on Autism" was its signal that autism will not be allowed to slip from the public awareness, like so many other feature stories that come and go. The simple truth has been unveiled, and anyone who looks can see it clearly: our prime question should not be asking how we can cure autism once it occurs. The evidence is now overwhelming that in most cases, this new epidemic that we call autism is a preventable disease.

DR. MERCOLA'S COMMENT:

Congratulations to Dr. O'Shea for an excellent review of this important topic.

Related Articles:

[Autism and Mercury Detoxification](#)

[Autism: a Novel Form of Mercury Poisoning](#)

[Studies on the Effects of Secretin in Children With Autism](#)

[Single Injection Of Secretin Does Not Treat Autism](#)

[Objections to the Study That Showed Secretin Does Not Work for Autism](#)

[Short-Term Benefit In Treating Autism With Antibiotics](#)

[The Neurobiology of Lipids In Autistic Spectrum Disorder](#)

[Link Between Autism and Vaccination](#)

[Autism May Be Caused By an Immune System Response To a Virus](#)

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[Milk Link To Autism](#)

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BARIUM

Barium is a trace element which can apparently affect thyroid function and which may be especially toxic for persons with thyroid disease, especially hyperthyroidism.

Barium sulfate (BaSO₄) is commonly used as a contrast medium in radiography of the intestinal tract. For these purposes a quite large amount is given orally to the person.

Barium carbonate (BaCO₄) is rat poison. This works by interfering with the sodium-potassium pump and causing a paralysis of the muscles, including the heart muscles and respiratory muscles, causing death.

Because barium interferes with the sodium-potassium pump, which seems already disturbed in hyperthyroidism, any ingestion of barium may be very toxic to someone with hyperthyroidism (or anyone for that matter).

Some hyperthyroids get periodic hypokalemic (potassium deficiency) paralysis from a deficiency of potassium or a reduced permeability of the muscles to potassium entry. Barium seems to cause the same reduced permeability to potassium and this may be its mode of toxicity.

Here are some pertinent studies:

STUDY 1:

Title

Periodic paralysis and the sodium-potassium pump.

Author

Layzer RB

Source

Ann Neurol, 11(6):547-52 1982 Jun

Abstract

Analysis of the pathophysiology of hypokalemic paralysis, as it occurs in **barium** poisoning, chronic potassium deficiency, and thyrotoxicosis, suggests that these disorders may have a similar mechanism. An increased ratio of muscle sodium permeability to potassium permeability reduces the ionic diffusion potential, while the resting membrane potential is sustained by an increase of Na-K pump electrogenesis. The result is that potassium entry (the sum of active and passive influx) exceeds potassium efflux; this causes a large shift of extracellular potassium into muscle until the Na-K pump turns off, leading to depolarization and paralysis. The primary defect in familial hypokalemic periodic paralysis, as in the example of **barium** poisoning, may be a marked reduction of muscle permeability to potassium.

STUDY 2:

Title

Hypokalemic paralyses: a review of the etiologies, pathophysiology, presentation, and therapy.

Author

Stedwell RE; Allen KM; Binder LS

Address

Department of Emergency Medicine, Texas Tech University Health Sciences Center, El Paso 79905.

Source

Am J Emerg Med, 10(2):143-8 1992 Mar

Abstract

Acute hypokalemic paralysis is an uncommon cause of acute weakness. Morbidity and mortality associated with unrecognized disease include respiratory failure and death. Hence, it is imperative for physicians to be knowledgeable about the causes of hypokalemic paralysis, and consider them diagnostically. The hypokalemic paralyses represent a heterogeneous group of disorders with a final common pathway presenting as acute weakness and hypokalemia. Most cases are due to familial hypokalemic paralysis; however, sporadic cases are associated with diverse underlying etiologies including thyrotoxic periodic paralysis, **barium** poisoning, renal tubular acidosis, primary hyperaldosteronism, licorice ingestion, and gastrointestinal potassium losses. The approach to the patient with hypokalemic paralysis includes a vigorous search for the underlying etiology and potassium replacement therapy. Further therapy depends on the etiology of the hypokalemia. Disposition depends on severity of symptoms, degree of hypokalemia, and chronicity of disease.

Study 3:

Food Addit Contam 1997 Jul;14(5):483-90

Preliminary assessment of potential health hazards associated with barium leached from glazed ceramicware.

Assimon SA, Adams MA, Jacobs RM, Bolger PM

Center for Food Safety and Applied Nutrition, US Food and Drug Administration, Washington, DC 20204, USA.

Ceramic glazes contain several elements which have the potential to leach into food or beverages that are held or stored in ceramicware. Recently, **barium** salts have been investigated as one of the alternatives to lead in frit formulations for glazes. This preliminary evaluation addresses the potential health hazards associated with **barium** at levels that might leach from glazed ceramicware. A set of specialty ceramicware, consisting of five teacups and a pitcher, was examined for extractable **barium**. Exposure to barium that adults (18-44 years) might encounter using the vessels for coffee, tea, or orange juice was estimated. The exposure estimate was derived from values for intakes of

the beverages and for the **barium** migration from glazed ceramicware test samples. An established reference dose (RfD) for barium exposure for the critical effect of hypertension was identified. The potential hazard associated with the leaching of **barium** from glazed ceramicware varied with the level of use. Consuming beverages in amounts up to the 95th percentile would not result in total **barium** intake in amounts that exceed the RfD; consuming large quantities (> 95th percentile) of beverages such as tea or coffee from glazed vessels might. This suggests that for a small portion of the population of users, intake of **barium** may be in quantities that warrant further consideration as a potential health hazard. Analyses of a broad sample of ceramicware and study of **barium** leaching behavior under actual use conditions are needed to assess further the significance of these findings.

PMID: 9328533, UI: 97469061

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OSTEOPOROSIS, BONE PROBLEMS, DENTAL PROBLEMS

Hyperthyroidism can be accompanied by some very bad dental problems. I went through some really bad periods where dental X-rays showed that my jaw bone was disintegrating. My teeth were loose and the tooth aches were incredible.

I managed to go from 1976 to 1998 without taking one single aspirin and only needed to take painkillers after hernia surgery. I hadn't taken any antibiotics for longer than that. But when I ran into hyperthyroidism induced dental problems I was forced into taking Tylenol around the clock and went through two sessions of taking antibiotics. It was really bad.

Consequently I know a little about dental problems which stem from hyperthyroidism. Also, you have probably heard that osteoporosis is a serious risk for hypers.

Calcium/magnesium metabolism gets seriously deranged in hyperthyroidism and it's essential to protect yourself from getting serious dental and bone problems.

Calcium and magnesium are also essential to control rapid heart rate. Many hypers use antithyroid medications and beta blockers to control the heart rate, but I didn't do this. I used calcium and magnesium.

I found early on that taking large doses of magnesium helped control the heart rate. Calcium and magnesium work together and neither should be taken for long without the other. I found that taking cal/mag in a 1:1 ratio worked very well for me to control my heart rate.

Dental and bone problems, however, tended to develop with a 1:1 ratio so I had to add some 2:1 ratio (cal to mag) to help control the tooth problems.

My serious dental problems developed when I tried to decrease the amount of cal/mag that I was taking. At the peak of the hyper episodes I was taking up to 36 capsules of cal/mag a day. This is 6000 mgs of each. Gradually I got that down to 3000 mgs. and that seemed to be a good amount for me.

When I tried to reduce the amount further is when I got the serious dental problems. I needed this much and I should have continued to take it until the need decreased.

Under the Supplements Page I wrote about the need to avoid taking large amounts of any one nutrient to prevent causing nutrient imbalances. Calcium and magnesium appear to be two minerals that do not cause imbalances of other minerals, perhaps because they are taken as a pair.

The ratio of calcium to magnesium may vary quite a bit for different people. One hyper woman in the group is taking much more magnesium than calcium and this works for her. You need to find the right ratio for you, and don't be surprised if this changes as you recover.

Teeth, and therefore probably bones, seem to need more calcium than the heart does. Calcium causes the heart to contract and magnesium makes it relax. In hyperthyroidism, we need more magnesium to keep the heart relaxed.

Bones and teeth, however, need more calcium. The 1:1 ratio of cal to mag may be great for the heart, but it may cause bone and teeth problems. I've found that it's best to have a 2:1 ratio supplement available also, in case tooth problems arise.

Recently I had a tooth ache develop. I had been having problems getting my calcium/magnesium balanced properly and had been experimenting with not taking any at all for several days at a time. I was able to get the tooth ache stopped in three days by the following 123 program:

1. FASTING AND 2:1 CALCIUM/MAGNESIUM

First I stopped eating anything--total fasting--with the exception of taking a 2:1 calcium/magnesium supplement. I would take as much as necessary for pain relief. Whenever I'd feel the pain increase, I would take 4-6 tablets and usually within 30 minutes the pain had subsided significantly.

2. RAW FOODS AND NO SALT (SODIUM)

I fasted for 36 hours and then commenced eating only raw foods. I ate celery first and then moved into salads with lettuce, avocado, tomato, and cucumber. I used absolutely no salt because salt (probably the sodium) interferes with calcium metabolism. You may find a great improvement in relieving tooth aches and muscle cramps from low calcium by avoiding salt.

3. AVOID SUGARS AND GRAINS

Next I avoided all sugars, even fruits, because sugars also interfere with calcium metabolism. By not eating any cooked foods, I also avoided grains (another negative for calcium).

By the third day, the tooth ache was 98% gone and I could start eating a small amount of fruit again. My need for the calcium/magnesium had significantly reduced and I felt much better than I had before I got the toothache.

I think that these steps are all important for preventing tooth and bone problems. In the long run, following these dietary practices can greatly reduce osteoporosis.

While you might not be able to go a long time on raw foods, it is a tremendous tool to regain balance, especially with cal/mag metabolism.

So when tooth or bone problems arise, or to prevent them: no salt, sugar, or cooked foods; take 2:1 cal/mag.

TEXTBOOK OSTEOPOROSIS INFORMATION

Williams' Textbook of Endocrinology, 9th Edition, 1998.

Bone is under a constant process of resorption and formation. As we age, formation lessens. After peak bone mass is achieved, bone mass remains stable (resorption and formation are equal). Excessive bone resorption (increased the most 5-15 years after menopause in women) is a reflection of increased activation frequency more than increased amount of bone resorbed.

The most common form of secondary osteoporosis is induced by exogenous glucocorticoids. This is particularly common in postmenopausal women, presumably because they have a tendency to develop primary osteoporosis and are more susceptible to the effects. However, fragility fractures can occur in any patient treated with glucocorticoids at moderate to high doses for a long period. In most instances of TED, glucocorticoids are used at small doses for short periods.

"Glucocorticoid induced osteoporosis is a result of both increased bone resorption and decreased bone formation. Increased resorption may be caused by decreased calcium absorption and the resulting secondary hyperparathyroidism. Decreased bone formation is probably caused by direct inhibition of osteoblasts, which are highly sensitive to glucocorticoids. (As little as 2.5 mg of prednisone at bedtime can block the normal nocturnal rise in osteocalcin, a hormone promoting bone formation.)."

"Hyperthyroidism can produce bone loss. In young people, however, the increase in bone formation is usually sufficient to offset the effects of resorption. If the disease is treated early, changes in bone mass are small."

As calcium is released from bone in hyperthyroidism, some patients will have excess serum calcium levels (hypercalcemia). This causes a decrease in parathyroid hormone (PTH). This low PTH interferes with the body's conversion of vitamin D (vitamin D is dependent on adequate PTH). Diminished intestinal absorption of vitamin D cause increased urinary calcium loss. The significance of this is that a slight increase in thyroid hormone levels can initiate this process. And this can ultimately result in osteoporosis. However, the thyroid also secretes the hormone calcitonin in response to high serum calcium levels. Calcitonin increases the activity of the bone producing cells known as osteoblasts and reduces activity of the osteoclasts, cells which break down bone. So the calcitonin tends to offset the effects of low PTH, etc. and the net effect is less than what was once thought. Of course, we're all different. Postmenopausal women in particular are more likely to be affected.

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BORON

Very little research has been done on boron and little is known about the symptoms of boron deficiency. Following we piece together a picture that indicates that boron is essential for magnesium and calcium metabolism, and is probably involved in estrogen and testosterone metabolism. There are a lot of reasons to suspect that a boron deficiency is involved in hyperthyroidism.

The following study suggests that boron works with magnesium and this may be one reason that it benefits persons with hyperthyroidism or persons with thyroid disease who are experiencing low magnesium symptoms like rapid heart rate and muscle cramping. You will note that boron both lessens the effects of a low magnesium diet but exacerbates deficiency symptoms. These seem to be the typical characteristics of when one nutrient works with another. Boron thus seems essential for magnesium metabolism and administration of boron will lower magnesium levels because it is enabling more of the magnesium to be utilized.

Another interesting observation in this study is that fructose mimics a magnesium deficiency, which reminds me of the studies on copper deficiency which showed that the symptoms of copper-deficiency are worse if the animal is also consuming fructose. We have seen that hypers have increased symptoms after eating fruit and this effect may be due to fructose increasing copper-deficiency symptoms. It would be very interesting to know how this fructose effect works--perhaps not by increasing copper deficiency itself but because it works like copper-deficiency in increasing the magnesium deficiency effects.

Magnes Res 2000 Mar;13(1):19-27

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Magnesium deficiency in the rat: effects of fructose, boron and copper.

Kenney MA, McCoy JH

School of Human Environmental Sciences, University of Arkansas, Fayetteville 72701, USA. kenney@comp.uark.edu

Magnesium (Mg) participates in many biochemical reactions which involve a variety of other nutrients. To elucidate some nutrient interactions, fructose (FR) and starch (ST) were compared as carbohydrate sources, and boron (B) and copper (Cu) were added to low-Mg diets for young male rats. Lack of Mg always caused characteristic deficiency symptoms. FR resembled Mg deficiency in effects on body, liver, and kidney weights and on plasma cholesterol level, but did not affect serum Mg or calcium (Ca). FR effects apparently were not mediated by changes in plasma Mg and Ca concentrations and were not prevented by adding Cu. **Boron appeared to lessen effects of a low-Mg diet on body growth, serum cholesterol, and ash concentration in bone, but exacerbated deficiency symptoms, without affecting the concentration of Mg or Ca in serum.** Results suggest that increased FR intake and marginal B might adversely affect individuals whose Mg status is suboptimal.

The following study, although enigmatic, appears to show that boron may affect thyroid function and the levels of T4 and T3.

Vopr Kurortol Fizioter Lech Fiz Kult 1989 May-Jun;(3):28-31

[Morphofunctional characteristics of the thyroid and a change in the level of thyroid hormones in the blood from the internal use of boron-containing waters].

[Article in Russian]

Korolev IuN, Panova LN, Bobkova AS, Korovkina EG

It has been established that intake of waters identical by Br concentrations (250 mg/l) but different by an ion-salt base leads to various structural changes of the thyroid at the tissue, cellular and subcellular levels. Artificial Br-containing water induces more pronounced shifts correlating with T3 and T4, blood concentrations. The ion-salt base was found essential in the mechanism of action of Br-containing water.

The following study shows that boron supplementation in males can increase estradiol (estrogen) and testosterone levels. This suggests that boron is involved in the conversion of progesterone into estradiol and testosterone. Since we have seen that hypers often have high progesterone levels and low estradiol levels (testosterone levels not known), this study offers more evidence that a boron deficiency may be involved in hyperthyroidism.

Biol Trace Elem Res 1997 Mar;56(3):273-86

The effect of boron supplementation on its urinary excretion and selected cardiovascular risk factors in healthy male subjects.

Naghii MR, Samman S

Department of Biochemistry, University of Sydney, NSW, Australia.

Boron (B) is an essential trace element for plants and its interrelationship with mineral and bone metabolism and endocrine function in humans has been proposed. Relatively little is known about the occurrence of B in the food chain and hence a biomarker which reflects

its intake is required. Two studies were carried out to quantify the urinary B concentration of subjects consuming their habitual diet and the effect of supplementation. In addition, the effect of supplementation on plasma lipoprotein cholesterol concentrations and susceptibility to oxidation and plasma steroid hormones were determined. Boron excretion, obtained on two different occasions from 18 healthy male subjects, was found to be in the range 0.35-3.53 mg/day, with no significant difference between the two occasions. Supplementation with 10 mg B/d for 4 wk resulted in 84% of the supplemented dose being recovered in the urine. Plasma estradiol concentrations increased significantly as a result of supplementation (51.9 +/- 21.4 to 73.9 +/- 22.2 pmol/L; $p < 0.004$) and there was a trend for plasma testosterone levels to be increased. However, there was no difference in plasma lipids or the oxidizability of low-density lipoprotein. Our studies suggest that the absorption efficiency of B is very high and estimation of the urinary B concentration may provide a useful reflection of B intake. In addition, the elevation of endogenous estrogen as a result of supplementation suggests a protective role for B in atherosclerosis.

The following study indicates that boron is involved in cognitive performance. Because of the observed decreases in mental functioning in thyroid disease it's important to consider all nutrients which may be involved in brain function. Also note that boron may be involved in membrane function. Since boron is a light element and many of the lighter elements are involved in the passage of the heavier elements through the cell walls, boron's function may be involved in this process. We have seen that other light elements like lithium perform functions regulating the passage of heavier elements like copper into the cells.

Environ Health Perspect 1994 Nov;102 Suppl 7:65-72

Dietary boron, brain function, and cognitive performance.

Penland JG

United States Department of Agriculture, Agricultural Research Service, Grand Forks, North Dakota 58202-9034.

Although the trace element boron has yet to be recognized as an essential nutrient for humans, recent data from animal and human studies suggest that boron may be important for mineral metabolism and membrane function. To investigate further the functional role of boron, brain electrophysiology and cognitive performance were assessed in response to dietary manipulation of boron (approximately 0.25 versus approximately 3.25 mg boron/2000 kcal/day) in three studies with healthy older men and women. Within-subject designs were used to assess functional responses in all studies. Spectral analysis of electroencephalographic data showed effects of dietary boron in two of the three studies. When the low boron intake was compared to the high intake, there was a significant ($p < 0.05$) increase in the proportion of low-frequency activity, and a decrease in the proportion of higher-frequency activity, an effect often observed in response to general malnutrition and heavy metal toxicity. Performance (e.g., response time) on various cognitive and psychomotor tasks also showed an effect of dietary boron. When contrasted with the high boron intake, low dietary boron resulted in significantly poorer performance ($p < 0.05$) on tasks emphasizing manual dexterity (studies II and III); eye-hand coordination (study II); attention (all studies); perception (study III); encoding and short-term memory (all studies); and long-term memory (study I). Collectively, the data from these three studies indicate that boron may play a role in human brain function and cognitive performance, and provide additional evidence that boron is an essential nutrient for humans.

The following study is a gold mine. The study shows that boron supplementation increases estradiol and testosterone and for reasons given above I believe that these results suggest that boron might be deficient in hyperthyroidism. Additionally boron was shown to decrease plasma concentrations of calcium. High calcium levels may be associated with increased heart rate. Since calcium and magnesium act as antagonists, this reduction of calcium by boron may allow magnesium levels to rise and thereby lower the heart rate and muscle cramps.

Additionally boron was shown to increase plasma copper, copper-zinc superoxide dismutase (SOD is one of the body's most important free radical scavengers), and ceruloplasmin (a protein which transports copper). Here is direct evidence that boron is essential for copper metabolism and therefore quite probably for the correction of hyperthyroidism and possibly hypothyroidism.

Furthermore, the study offers a possible explanation for why estrogen may slow thyroid function: it increases plasma copper, SOD, and ceruloplasmin. Boron also increased these variables whether estrogen was administered or not.

This is excellent documentation to support my observations that boron was important in my recovery from hyperT.

Environ Health Perspect 1994 Nov;102 Suppl 7:59-63

Biochemical and physiologic consequences of boron deprivation in humans.

Nielsen FH

United States Department of Agriculture, Agricultural Research Service, Grand Forks, North Dakota 58202-9034.

Boron deprivation experiments with humans have yielded some persuasive findings for the hypothesis that boron is an essential nutrient. In the first nutritional study with humans involving boron, 12 postmenopausal women first were fed a diet that provided 0.25 mg boron/2000 kcal for 119 days, and then were fed the same diet with a boron supplement of 3 mg boron/day for 48 days. **The boron supplementation reduced the total plasma concentration of calcium and the urinary excretions of calcium and magnesium, and elevated the serum concentrations of 17 beta-estradiol and testosterone.** This study was followed by one in which five men over the age of 45, four postmenopausal women, and five postmenopausal women on estrogen therapy were fed a boron-low diet (0.23 mg/2000 kcal) for 63 days, then fed the same diet supplemented with 3 mg boron/day for 49 days. The diet was low in magnesium (115 mg/2000 kcal) and marginally adequate in copper (1.6 mg/2000 kcal) throughout the study. **This experiment found higher erythrocyte superoxide dismutase, serum enzymatic ceruloplasmin, and plasma copper during boron repletion than boron depletion.** The design of the most recent experiment was the same as the second study, except this time the diet was adequate in magnesium and copper. **Estrogen therapy increased plasma copper and serum 17 beta-estradiol concentrations; the increases were depressed by boron deprivation. Estrogen ingestion also increased serum immunoreactive ceruloplasmin and erythrocyte superoxide dismutase; these variables also were higher during boron repletion than depletion for all subjects, not just those ingesting estrogen.**

The following study indicates that boron and molybdenum affect estrogen metabolism and concludes that "It is possible that high dietary intakes of boron or molybdenum could regulate the rate of catabolism, or even the metabolic fate of the major estrogens."

J Inorg Biochem 1992 May 15;46(3):153-60

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Borate and molybdate inhibition of catechol estrogen and pyrocatechol methylation by catechol-O-methyltransferase.

Beattie JH, Weersink E

Division of Biochemical Sciences, Rowett Research Institute, Bucksburn, Aberdeen, U.K.

The possibility that boron and molybdenum anions can influence sex steroid metabolism by forming complexes with catechol estrogens has been studied in vitro. The formation of 2-methoxyestrone (2-OHE1 2-Me) from 2-hydroxyestrone (2-OHE1) by catechol-O-methyltransferase (COMT) was followed by measuring the transfer of the radiolabeled methyl group from S-adenosylmethionine. In the presence of both sodium tetraborate and sodium molybdate using a phosphate buffer medium, the formation of 2-OHE1 2-Me decreased as the anion:2-OHE1 molar ratio was increased. However, the reverse effect was observed when using a tris buffer medium and further investigation showed that phosphate and sulphate also enhanced COMT activity in a tris buffer medium. Boric acid affinity medium, used as a substitute for borate salt, also showed a negative relationship with enzyme activity in a phosphate buffer medium, and inhibition of methylation was more marked than with the free anion. Erythrocytes contain appreciable amounts of COMT, which is mostly responsible for the rapid O-methylation of catechol estrogens in blood. The methylation of a simple catechol compound, 1,2-dihydroxybenzene (pyrocatechol) was therefore studied using rat red blood cell lysates. Methylation was inhibited in a concentration-related manner by borate, as found in the studies of 2-OHE1. It is possible that high dietary intakes of boron or molybdenum could regulate the rate of catabolism, or even the metabolic fate of the major estrogens.

This is the original USDA study which showed that boron supplementation increases estrogen and testosterone in postmenopausal women. The study also showed that boron "markedly reduced the urinary excretion of calcium and magnesium," interacts with magnesium metabolism, and the boron effects were not negated by a high intake of aluminum (1000 mg per day). It seems as though boron conserves magnesium and calcium, prevents the bone demineralization, and protects against osteoporosis.

FASEB J 1987 Nov;1(5):394-7

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Effect of dietary boron on mineral, estrogen, and testosterone metabolism in postmenopausal women.

Nielsen FH, Hunt CD, Mullen LM, Hunt JR

United States Department of Agriculture, Grand Forks Human Nutrition Research Center, North Dakota 58202.

A study was done to examine the effects of aluminum, magnesium, and boron on major mineral metabolism in postmenopausal women. This communication describes some of the effects of dietary boron on 12 women between the ages of 48 and 82 housed in a metabolic unit. A boron supplement of 3 mg/day markedly affected several indices of mineral metabolism of seven women consuming a low-magnesium diet and five women consuming a diet adequate in magnesium; the women had consumed a conventional diet supplying about 0.25 mg boron/day for 119 days. **Boron supplementation markedly reduced the urinary excretion of calcium and magnesium;** the depression seemed more marked when dietary magnesium was low. Boron supplementation depressed the urinary excretion of phosphorus by the low-magnesium, but not by the adequate-magnesium, women. **Boron supplementation markedly elevated the serum concentrations of 17 beta-estradiol and testosterone; the elevation seemed more marked when dietary magnesium was low. Neither high dietary aluminum (1000 mg/day) nor an interaction between boron and aluminum affected the variables presented.** The findings suggest that supplementation of a low-boron diet with an amount of boron commonly found in diets high in fruits and vegetables induces changes in postmenopausal women consistent with the prevention of calcium loss and bone demineralization.

Additional studies on boron:

Boron is an essential nutrient for certain organisms, notably vascular plants and diatoms. Cyanobacteria require boron for formation of nitrogen-fixing heterocysts and boron may be beneficial to animals. Boron deficiency in plants produces manifold symptoms: many functions have been postulated. Deficiency symptoms first appear at growing points, within hours in root tips and within minutes or seconds in pollen tube tips, and are characterized by cell wall abnormalities. Boron-deficient tissues are brittle or fragile, while plants grown on high boron levels may have unusually flexible or resilient tissues. Borate forms cyclic diesters with appropriate diols or polyols. The most stable are formed with cis-diols on a furanoid ring. Two compounds have this structure physiologically: ribose in ribonucleotides and RNA, and apiose in the plant cell wall. **Germanium** can substitute for boron in carrot cell cultures. Both boron and **germanium** are localized primarily in the cell wall. We postulate that borate-apiofuranose ester cross-links are the auxin-sensitive acid-growth link in vascular plants, that the cyanobacterial heterocyst envelope depends on borate cross-linking of mannopyranose and/or galactopyranose residues in a polysaccharide-lipid environment, and that boron in diatoms forms ester cross-links in the polysaccharide cell wall matrix rather than boron-silicon interactions. Complexing of ribonucleotides is probably a factor in boron toxicity. [boron--chemistry and biology.doc](#)

Interest in boron as a naturally occurring trace element nutrient from the food supply is increasing. Mounting evidence suggests that boron is essential to human beings. This study explores the major food and beverage contributors of boron and estimates of daily boron intake from the American diet. Previous estimates in the literature of dietary boron consumption are based on limited foods and population segments. In this study we provide a more comprehensive assessment of boron consumption by the US population. A boron nutrient database of 1,944 individual foods was developed. These foods represent 95.3% by weight of all foods consumed in the US Department of Agriculture 1989-1991 Continuing Survey of Food Intakes by Individuals (1989-1991 CSFII). The Boron Nutrient Database (version 1.0) was then linked to the 3-day food records of 11,009 respondents to the 1989-1991 CSFII to generate the average daily boron intake for each person. The weighted 5th percentile, median, mean, and 95th percentile boron intakes, respectively, are 0.43, 1.02, 1.17 and 2.42 mg/day for men; 0.33, 0.83, 0.96 and 1.94 mg/day for women; and 0.40, 0.86, 1.01 and 2.18 mg/day for pregnant women. For vegetarian adults, these intakes are 0.46, 1.30, 1.47 and 2.74 mg/day for men and 0.33, 1.00, 1.29 and 4.18 mg/day for women. The top 2 boron contributors, coffee and milk, are low in boron, yet they make up 12% of the total boron intake by virtue of the volume consumed. Among the top 50 boron contributors, peanut butter, wine, raisins, peanuts, and other nuts are high in boron. As more data become available on daily boron requirements, the results of this study may be used to assess whether Americans' daily intake of boron is adequate. [boron--daily intake in American diet.doc](#)

Biol Trace Elem Res 1998 Winter;66(1-3):319-30

The justification for providing dietary guidance for the nutritional intake of boron.

Nielsen FH

United States Department of Agriculture, Agricultural Research Service, Grand Forks Human Nutrition Research Center, ND 58202-9034, USA.

Because a biochemical function has not been defined for boron (B), its nutritional essentiality has not been firmly established. Nonetheless, dietary guidance should be formulated for B, because it has demonstrated beneficial, if not essential, effects in both animals and humans. Intakes of B commonly found with diets abundant in fruits, vegetables, legumes, pulses, and nuts have effects construed to be beneficial in macromineral, energy, nitrogen, and reactive oxygen metabolism, in addition to enhancing the response to estrogen therapy and improving psychomotor skills and cognitive processes of attention and memory. Perhaps the best-documented beneficial effect of B is on calcium (Ca) metabolism or utilization, and thus, bone calcification and maintenance. The paradigm emerging for the provision of dietary guidance that includes consideration of the total health effects of a nutrient, not just the prevention of a deficiency disease, has resulted in dietary guidance for chromium (Cr) and fluoride; both of these elements have beneficial effects in humans, but neither has a defined biochemical function. Knowledge of B nutritional effects in humans equals or is superior to that of Cr and fluoride; thus, establishing a dietary reference intake for B is justified. An analysis of both human and animal data suggests that an acceptable safe range of population mean intakes of B for adults could well be 1-13 mg/d. Recent findings indicate that a significant number of people do not consistently consume more than 1 mg B/d; this suggests that B could be a practical nutritional or clinical concern.

Biol Trace Elem Res 1988 Sep-Dec;17:91-107

Magnesium and methionine deprivation affect the response of rats to boron deprivation.

Nielsen FH, Shuler TR, Zimmerman TJ, Uthus EO

US Department of Agriculture, Grand Forks Human Nutrition Research Center, ND 58202.

A series of nine experiments were done to obtain further evidence that boron might be involved in major mineral metabolism (Ca, P, and Mg), thus indicating that boron is an essential nutrient for animals. Eight factorially arranged experiments of 6-10 wk durations were done with weanling Sprague-Dawley male rats. One factorially arranged experiment was done with weanling spontaneously hypertensive rats. The variables in each experiment were dietary boron supplements of 0 and 3 micrograms/g, and dietary magnesium supplements of either 200 (Experiments 1-3) or 100 (Experiments 4-9) and 400 micrograms/g. In Experiments 7 and 9, a third variable was dietary manganese supplements of 25 and 50 micrograms/g. Methionine status was varied throughout the series of experiments by supplementing the casein-based diet with methionine and arginine. Findings were obtained indicating that the severity of magnesium deprivation and the methionine status of the rat strongly influence the extent and nature of the interaction between magnesium and boron, and the response to boron deprivation. When magnesium deprivation was severe enough to cause typical signs of deficiency, a significant interaction between boron and magnesium was found. Generally, the interaction was characterized by the deprivation of one of the elements making the deficiency signs of the other more marked. The interaction was most evident when the diet was not supplemented with methionine and especially when the diet contained luxuriant arginine. Signs of boron deprivation were also more marked and consistent when the diet contained marginal methionine and luxuriant arginine. Among the signs of boron deprivation exhibited by rats fed marginal methionine were depressed growth and bone magnesium concentration, and elevated spleen wt/body wt and kidney wt/body wt ratios. Because the boron supplement of 3 micrograms/g did not make the dietary intake of this element unusual, it seems likely that the response of the rats to dietary boron in the present study were manifestations of physiological, not pharmacological, actions, and support the hypothesis that boron is an essential nutrient for the rat.

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CALCIUM AND MAGNESIUM

Calcium and magnesium are extremely important minerals that are often out of balance in persons with thyroid disease. Imbalances of these minerals can result in very rapid heart rate, low heart rate, and irregular heart rate. Thyroid function itself is most likely controlled by the ratio of these minerals.

Most people with thyroid disease find that they have to supplement calcium and magnesium. Supplementing these minerals in the correct ratio can make a huge improvement in the symptoms. However, supplementing them in the wrong ratio can make symptoms worse. To further complicate the situation, the correct ratio of cal/mag changes as you recover from thyroid disease.

I have struggled a very long time with finding the right cal/mag ratio for myself. Well after recovering from hyperthyroidism, swinging back hypo, and then getting normal again, I had many months of fast, irregular heart rate that was often initiated by strenuous exercise. Because magnesium had been an important factor in reducing my heart rate when I was hyper, I would take a cal/mag supplement in a 1:1 ratio or take 400-800 mgs of magnesium only to correct this problem. Usually I would have this irregular heart rate throughout the night but would be recovered by morning.

I experimented with potassium and found that taking 800-1200 mgs of potassium before my night time basketball often prevented the irregular heart rate and began thinking that I was potassium deficient. One time I grabbed an unlabeled baggie that I thought was potassium and took 6 capsules before playing. I had extreme irregular heart rate that lasted all night. I later discovered that I had mistakenly taken magnesium.

This was very strange to me because magnesium had been my savior for such a long time. Whenever I had high heart rate when I was hyper, magnesium would slow my heart, usually within 20-30 minutes. So I was wondering, "Why doesn't it work now?" I began to think that the manufacturer had made a mistake and there was a problem with the product.

Eventually the answer came in a sudden insight. I was lying awake at night with my heart beating very irregular and fast. Paying close attention to my heart, I realized that my heart was not just irregular and fast, it was beating very weakly. I noted that this was in stark contrast to the time when I was hyper. Then my heart was beating fast and irregular, but very strong.

The insight was that it was the strength of my heart beat and not the speed and irregularity that was the key. I thought back on how calcium is the mineral that is responsible for the heart contracting and magnesium is responsible for the heart relaxing.

During hyperthyroidism, magnesium is low and calcium is high. This imbalance is the result of other mineral imbalances (copper, zinc, iron, etc.), but the effects on the heart rate are direct effects of a calcium/magnesium imbalance. This can be demonstrated by taking a magnesium supplement or a cal/mag supplement with much higher magnesium than the usual 2:1 cal/mag ratio when your heart rate is high. This intake of more magnesium will slow the heart rate temporarily. However, as we have seen, the body can't maintain normal magnesium levels in the blood if copper is low. So until copper is replenished, extra magnesium is needed on a constant basis to control the rapid heart rate.

The key to understanding the effects of calcium and magnesium on the heart is this: Calcium is needed for muscles to contract and magnesium is needed for muscles to relax. The heart muscles are like all muscles. Calcium causes heart contraction; magnesium causes heart relaxation.

If magnesium is low, as during hyperthyroidism, and calcium is adequate, the heart contracts normally but the relaxation phase is shortened and incomplete. If the normal heart contracts for .5 seconds and relaxes for .5 seconds, we have a 1.0 second cycle which translates into a 60 beats per minute heart rate. If magnesium is low and the relaxation phase is shortened to .25 seconds, then the complete cycle is .75 seconds, which translates to a 80 beats per minute heart rate (60 seconds divided by .75 seconds). As you can see, as magnesium gets more depleted, the relaxation phase shortens and the heart rate increases.

When I was experiencing the irregular heart rate, what was happening was that it was calcium that was low and not magnesium. When calcium is low, the contraction phase is shortened while the relaxation phase remains normal. If the contraction phase shortens to .25 seconds and the relaxation phase stays at .5 seconds, the heart rate also increases to 80 beats per minute. If you just looked at the increase in rate, you might, as I did, think that magnesium was deficient.

The key to the insight that it was calcium that was deficient was the observation that the heart rate was weak. A weak heart rate means that calcium is deficient and the contraction phase is weak and short. This results in an increase in heart rate and also an irregular heart rate because some contractions are missed entirely. Contrast this to a magnesium deficiency where the heart rate is irregular because some of the relaxations are missed.

Once I reached this insight, it all became so simple. I was amazed that I had continued to make the same mistake over and over again. The key mental block for me was that I thought that magnesium always slowed and regulated the heart rate. Once I thought through the whole process of how calcium and magnesium affect

the heart, I realized that a calcium deficiency can also lead to a fast and irregular heart rate.

With this new insight, I switched my cal/mag ratio to 2:1. I had been mixing a 1:1 ratio supplement with a 2:1 supplement which resulted in a ratio of about 3:2. However with the addition of extra magnesium or extra 1:1 cal/mag after basketball, I probably had about a 1:1 overall ratio.

Once I switched to a 2:1 ratio, the heart irregularity completely disappeared and hasn't occurred in months. I found that the cal/mag ratio is the key. However along the way to this discovery I ran across some other interesting information.

As I was struggling through this irregular heart rate problem, I found that two things often helped the situation: potassium and vitamin B-5. Potassium often helped and I think the reason for this is that potassium and magnesium are antagonistic minerals. Since I was essentially suffering from too much magnesium (or too little calcium), the potassium helped because it reduced the metabolic effect of the magnesium (or assisted the metabolism of calcium). I think this is important, particularly for persons with hypothyroidism, because they need a higher calcium to magnesium ratio. A potassium deficiency could prevent the cells from getting enough calcium which is an activator in the cellular response to thyroid hormone.

The other discovery was that vitamin B-5 is important in preventing irregular heart rate. If B-5 gets deficient, it seems to have an effect on the calcium/magnesium metabolism so that calcium doesn't work as well. A B-5 deficiency has similar effects to a calcium deficiency. I don't know why this happens, but I now realize that it's important when supplementing B complex vitamins to always make sure that you are taking as much B-5 as any of the other B vitamins. For example, if you are supplementing with high amounts of niacin (for headaches or other reasons), be aware that you will need to increase B-5 to the same amount or a little greater to prevent a disturbance of the cal/mag ratio which could result in irregular heart rate.

One other discovery in all this was that by not taking enough calcium and taking too much magnesium, another of my teeth died. I developed an extreme tooth ache which led to another root canal. For dental and bone health, don't maintain a high magnesium/calcium ratio past the point where you need it.

Remember that balancing calcium and magnesium won't correct thyroid problems. You'll need to correct the other minerals like copper, zinc, iron, selenium, chromium, manganese, etc. to achieve this. Calcium and magnesium get out of balance because of these other nutritional problems. However, getting your calcium/magnesium balance corrected is essential for normalizing heart rate, preventing dental decay and osteoporosis, and preventing muscle cramps (too little magnesium).

In summary, to balance calcium and magnesium keep these points in mind: a normal person need a cal/mag ratio of about 2:1; a hyper needs more magnesium and a hypo needs more calcium, but these ratios need to be constantly adjusted as you approach normality; irregular heart rate can be a sign of either too little calcium or too little magnesium; the key to knowing whether you need calcium or magnesium is the strength of the heart beat, not the speed or the irregularity--if it's too strong, take more magnesium and if it's too weak, take more calcium.

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CADMIUM

Cadmium appears to be the largest single contributor to autoimmune thyroid disease. It is a very powerful and toxic metal which seems to be placed at the very center of the thyroid story. I think you'll find this file very interesting.

Not only does cadmium appear to play a very pivotal role in thyroid disease, it is a very unique mineral. It is extremely toxic and has toxic biological effects at concentrations smaller than almost any commonly found mineral.

Despite this great toxicity, there is some evidence that cadmium is an essential nutrient with biological function. We will be exploring this dichotomy of cadmium.

One of the greatest effects of cadmium is that it depletes selenium in the body because selenium is essential for cadmium removal. Selenium atoms combine with cadmium atoms and are escorted out of the body via the bile system. When selenium is depleted by cadmium, there is less selenium to form the deiodinase enzymes which convert T4 to T3, resulting in low T3 and hypothyroidism. Also there is less selenium to form glutathione peroxidase, one of the body's prime antioxidants. This results in greater levels of reactive oxygen species and hydrogen peroxide, which lead to an increased production of thyroid hormone and damage to the thyroid gland.

The following study shows that cadmium and mercury toxicities (at high levels) will induce immediate hyperthyroidism.

Title

Thyrototoxicity of the chlorides of cadmium and mercury in rabbit.

Author

Ghosh N; Bhattacharya S

Address

Department of Zoology, Visva-Bharati University, Santiniketan, India.

Source

Biomed Environ Sci, 5(3):236-40 1992 Sep

Abstract

Exposure to heavy metals such as cadmium and mercury is of immediate environmental concern. The present study was aimed at establishing a direct relationship between heavy metal poisoning and thyroid dysfunction. Cadmium and mercury treatment at LD50 levels resulted in severe thyrotoxicosis in the rabbit. Within 24 h of intramuscular administration of cadmium chloride 15 mg.kg-1 body weight (bw) and mercury chloride 20 mg.kg-1 bw, thyroid peroxidase activity increased significantly over the control with a concomitant rise in the triiodothyronine (T3) titre. On the other hand, there was a remarkable fall in the thyroxine (T4) level, and the T3/T4 ratio was high as compared with the control. Evidence indicates that acute heavy metal lethality will induce immediate hyperthyroidism. It is suggested that T3-toxicosis may be produced by a preferential synthesis of T3 and/or preferential deiodination of T4 to T3. Measurement of T3 and T4 levels may thus be utilized as a reliable indicator of heavy metal lethality.

The following study examines the thyroidal functioning of inhabitants of a cadmium polluted river basin in Japan. Free T4 levels are found to be lower than normals but T3 levels are higher.

Title

[A study of thyroid hormone levels of inhabitants of the cadmium-polluted Kakehashi River basin]

Author

Nishijo M; Nakagawa H; Morikawa Y; Tabata M; Senma M; Miura K; Tsuritani I; Honda R; Kido T; Teranishi H; et al

Address

Department of Public Health, Kanazawa Medical University, Ishikawa, Japan.

Source

Nippon Eiseigaku Zasshi, 49(2):598-605 1994 Jun

Abstract

We compared thyroid hormone levels of inhabitants (19 men and 16 women) of the cadmium (Cd)-polluted Kakehashi River basin in Ishikawa Prefecture, with those of subjects (23 men and 47 women) living in a non-polluted area. In addition, we investigated the relationships between the thyroid hormone levels and indices of renal dysfunction induced by Cd exposure. The following results were obtained: 1) The free T4 level of females was significantly lower than that of controls. 2) The T3 level of inhabitants of both sexes was significantly higher than that of controls. 3) The level of free T4 among females became lower with the increases of urinary beta 2-microglobulin (beta 2-MG), urinary protein, urinary sugar, urinary amino acids and serum creatinine (Cr) levels, and with decreases of creatinine-clearance (CCr) and %TRP. 4) We could not find any relationship between the increase of T3 and the indices of renal dysfunction induced by Cd exposure in either sex.

The following study shows that cadmium decreases T3 by interfering with T4 to T3 conversion.

Environ Res 1987 Apr;42(2):400-5

[S](#)

Effect of cadmium on T4 outer ring monodeiodination by rat liver.

Yoshida K, Sugihira N, Suzuki M, Sakurada T, Saito S, Yoshinaga K, Saito H

The effect of cadmium on thyroxine (T4) outer ring monodeiodination was studied in vivo and in vitro in the rat liver. One microgram of T4 was incubated with rat liver homogenates in 50 mM Tris--HCl buffer, pH 7.4, with or without 0.5, 5, and 50 mM dithiothreitol (DTT) for 60 min in the presence of 10⁻⁸ to 10⁻³ M CdCl₂, and the

amount of 3,5,3'-triiodothyronine (T3) produced was determined by a specific radioimmunoassay. Subcutaneous injection of CdCl₂, 1 mg/kg BW/day, 5 days a week for 10 weeks, to the rats resulted in a significant reduction in serum T3 concentration (by 37%) and hepatic T3 production from T4 (by 78 to 92%). In vitro addition of 1 microM to 1 mM CdCl₂ to liver homogenates caused a concentration-dependent reduction in T3 generation. Without DTT a 50% reduction in the T4 to T3 converting activity was caused by 4 X 10⁻⁶ M CdCl₂. DTT (0.5 to 50 mM) partially restored T3 generation roughly in a concentration-dependent manner. These results indicate that cadmium has some effects on the metabolism of thyroid hormone.

The following study demonstrates the existence of a cadmium-binding protein (CdBP) in human thyroid tissue but not in dogs, pigs, and oxen. Cadmium accumulates in the thyroid, kidney, liver, and pancreas—all areas that seem to be involved in thyroid disease.

Toxicol Lett 1982 May;11(3-4):269-73

Cadmium-binding proteins in human organs.

Sato M, Takizawa Y

Cadmium-binding proteins (CdBPs) in the cytosol fractions from several organs of man orally exposed to cadmium (Cd) were examined by gel chromatography. In kidney and liver most of the cadmium (76-87%) in the cytosols was bound to metallothionein, and hepatic metallothionein contained zinc also at a similar level. The pancreas cytosol also contained a metallothionein-like CdBP, although its content was only one-tenth of the hepatic one. **In the thyroid gland a prominent CdBP, eluting later than that of metallothionein, was observed; this CdBP was not detectable in normal dogs, pigs, and oxen.** No CdBPs were observed in other organs including heart, muscle, genital organs, aorta, and bone. **These results suggest that CdBPs participate in accumulation and distribution of cadmium in man, since organs containing CdBP such as kidney, liver, pancreas, and thyroid gland show a tendency to accumulate high levels of cadmium.**

The following study indicates that cadmium may inhibit lipogenesis by binding with the thiol group (SH) of coenzyme A, thereby reducing the serum levels of free fatty acids and lipid peroxides. Keep in mind that all antithyroid drugs all have this thiol group and providing this may be their mode of action. Intriguingly, cadmium was found to have different effects in males and females in regard to the effects on fatty acids. This may be a possible mechanism to explain why females get thyroid diseases at a much higher rate than males. Also interesting is that cadmium by interfering with the action of the thiol group may be interfering with the metabolism of vitamin D and possibly the conversion of cholesterol into the steroid (sex) hormones. This may explain how cadmium increases osteoporosis, a phenomenon demonstrated by osteoporosis in older smokers, especially women.

Title

[Effect of cadmium on lipid components: relation of cadmium to thyroid hormone and growth hormone]

Author

Fujita D

Address

Department of Public Health, Hyogo College of Medicine, Nishinomiya.

Source

Nippon Eiseigaku Zasshi, 47(3):704-14 1992 Aug

Abstract

To clarify the relationship of **cadmium** (Cd), thyroid hormone (TH) and growth hormone (GH) to lipid components, 4-week-old SD rats were dosed orally with Cd (CdCl₂) at a dose of 2.0 mg/kg body weight five times a week, orally with TH at a dose of 2.5 mg/kg body weight five times a week and subcutaneously with GH (somatotropin) at a dose of 1.0 IU/kg body weight three times a week, all for 4 weeks. As lipid components, the serum concentrations of triglycerides, free fatty acids, lipid peroxides and long-chain fatty acids were determined. We have devised a new method for determining the fatty acid composition in the femur using gas chromatography-mass spectrometry and made a simultaneous analysis of fatty acids, from myristic acid (C14:0) to cholesterol. The results of the present study led to the following conclusions. 1. **Cd may inhibit lipogenesis by binding with SH of coenzyme A, thereby reducing the serum levels of free fatty acids and lipid peroxides.** 2. **When TH and Cd were administered in combination, the addition of Cd produced an inhibitory effect on lipid components, although TH given alone stimulated the lipid metabolism. Therefore, Cd and TH may have an interaction in lipid components.** 3. **When GH and Cd were administered in combination, Cd modulated the action of GH, which enhanced the effect of somatomedin on the lipid metabolism. The inhibitory effect of Cd on somatomedin activity via Zn was suggested.** 4. **A sex difference was found in the composition of fatty acids in blood. The males had higher proportions of palmitic acid (C16:0) and linoleic acid (C18:2), while the females had a higher proportion of arachidonic acid (C20:4).** There was no sex difference in fatty acid composition in the femur. 5. **It was confirmed that TH produced a peroxide of dehydrocholesterol, a precursor of vitamin D3, in the diaphysis of the femur in the increased metabolic state.**

The following study indicates how cadmium enters the food chain. Cadmium waste from industrial production is disposed in the sewers and the sewage sludge is used for agricultural fertilizer. Also there is an indication that cadmium might be present in phosphate fertilizers since it is used in their manufacture. If this is true then virtually all non-organically grown foods are going to have higher than normal amounts of cadmium.

Title: Sources of cadmium in the environment.

Author

Hutton M

Source

Ecotoxicol Environ Saf, 7(1):9-24 1983 Feb

Abstract

This paper is concerned with quantifying the major sources of **cadmium** in the European Community and assessing the relative significance of such inputs to the environmental compartments, air, land, and water. The methodology involved identification of

potential sources of **cadmium**, including natural processes, as well as those associated with human activities. This was followed by a review of any emission studies of these processes and subsequent estimation of an emission factor for each source. The emission factor was applied to the most recent production or consumption data for the process in question to obtain an estimate of the annual discharge. The steel industry and waste incineration, followed by volcanic action and zinc production, are estimated to account for the largest emissions of atmospheric **cadmium** in the region. **Waste disposal results in the single largest input of cadmium to land; the quantity of cadmium associated with this source is greater than the total from the four other major sources—coal combustion, iron and steel production, phosphate fertilizer manufacture and use, and zinc production.** The characterization of **cadmium** inputs to aquatic systems is incomplete but of the sources considered, the manufacture of **cadmium**-containing articles accounts for the largest discharge, followed by **phosphate fertilizer manufacture and zinc production.**

To me the following study is another indication that cadmium is a selenium antagonist. Since arsenic is just to the left of selenium in the Periodic Table and is known to be a selenium antagonist, it's not surprising that when arsenic and cadmium (also a selenium antagonist) are combined there is an increased combined effect of reducing selenium and glutathione.

Title

Arsenic-cadmium interaction in rats: toxic effects in the heart and tissue metal shifts.

Author

Y'a~nez L; Carrizales L; Zanatta MT; Mej'ia JJ; Batres L; D'iaz-Barriga F

Address

Departamento de Bioqu'ímica, Facultad de Medicina, Universidad Aut'onoma de San Luis Potos'í, Mexico.

Source

Toxicology, 67(2):227-34 1991 Apr 8

Abstract

Previously, we had shown that arsenic interacts with **cadmium** in rats; our results showed that the toxicity of a mixture of arsenic + **cadmium** cannot be predicted by the toxic mechanisms of the individual components. In this paper, we present further evidence about the interaction of arsenic and **cadmium** in rats. The results were: arsenic modified the 24 h-LD50 value of **cadmium** more clearly than **cadmium** did with the one of arsenic; based on the LD50 values, the mixtures we studied were more toxic than either metal alone. With single doses (As 10 mg/kg, Cd 2.6 mg/kg, and As 10 mg/kg + Cd 2.6 mg/kg) the mixture As + Cd was more toxic than each metal. At these doses, **cadmium** significantly induces the levels of glutathione, metallothionein, and lipid peroxidation in heart tissue, as compared to a saline group of rats. Arsenic incremented glutathione and lipid peroxidation at higher values than those obtained with **cadmium**. The mixture of As + Cd behaved as arsenic in the induction of lipid peroxidation and glutathione and like **cadmium** in metallothionein induction. Finally, rats treated with As + Cd had less Cd in liver than animals treated only with **cadmium**, and more As in heart tissue than rats treated only with arsenic. Our results give further evidence about the arsenic-**cadmium** interaction in rats, demonstrate the utility of employing different biomarkers in the study of chemical mixtures and indicate that heart tissue is affected not only by the mixture of As + Cd, but also by either metal alone.

The following study shows that while cadmium seems not to affect progesterone levels it does decrease estrogen (estradiol) levels. My suspicion is that cadmium accomplishes this by decreasing copper levels and that copper is essential for the conversion of progesterone to estrogen.

Title

Cadmium interferes with steroid biosynthesis in rat granulosa and luteal cells in vitro.

Author

Paksy K; Varga B; L'az'ar P

Address

National Institute of Occupational Health, Budapest, Hungary.

Source

Biometals, 5(4):245-50 1992 Winter

Abstract

Recently, cadmium has been described to disturb ovarian function in rats. In this paper the direct influence of **cadmium** on steroid production of ovarian cells in vitro has been studied. Granulosa and luteal cells were obtained from proestrous and pregnant rats, and incubated with 0, 5, 10, 20 or 40 micrograms ml⁻¹ CdCl₂ in the presence or absence of 0.1-1000 ng ml⁻¹ follicle stimulating hormone (FSH) or luteinizing hormone (LH) for 24 or 48 h. **Production of progesterone (P) and 17 beta-estradiol (E2)** by granulosa and that of P by luteal cells were measured by radioimmunoassay. In FSH-stimulated granulosa cell cultures, 5 and 40 micrograms ml⁻¹ CdCl₂ suppressed P accumulation to 65 and 10%, respectively; accumulation of E2 (at 5 micrograms ml⁻¹ CdCl₂) decreased to 44%. P production of LH-supported luteal cells dropped to 86 and 66%, respectively, when 5 and 40 micrograms ml⁻¹ CdCl₂ was added to the medium. **No alteration in basal P accumulation** occurred in granulosa and luteal cell cultures following incubations with 20 and 40 micrograms ml⁻¹ CdCl₂, **whereas basal E2 production of granulosa cells was markedly diminished. It is concluded that CdCl₂ suppressing steroid synthesis in vitro exerts a direct influence on granulosa and luteal cell function.**

The following study indicates that cadmium causes emphysema, a disease characterized by extensive disruption of lung connective tissue, by inhibiting the production of connective tissue proteins (collagen).

Title

Cadmium inhibits proteoglycan and procollagen production by cultured human lung fibroblasts.

Author

Chambers RC; Laurent GJ; Westergren-Thorsson G

Address

Centre for Cardiopulmonary Biochemistry and Respiratory Medicine, University College Medical School, Rayne Institute, London, United Kingdom. R.Chambers@ucl.ac.uk

Source

Am J Respir Cell Mol Biol, 19(3):498-506 1998 Sep

Abstract

Chronic inhalation of cadmium at the workplace or in cigarette smoke is associated with emphysema, a disease characterized by extensive disruption of lung connective tissue. We have previously shown that cadmium, at noncytotoxic doses, inhibits fibroblast procollagen production in vitro, with maximal inhibitory effects of 69 +/- 6% (P < 0.01) at 30 µM **cadmium** chloride (CdCl₂). In this paper we show that at similar doses, **cadmium also inhibits proteoglycan synthesis**, with values reduced by between 36 +/- 4% (P < 0.01) and 42 +/- 6% (P < 0.01) for proteoglycans secreted into the culture media and associated with the cell layer, respectively. The greatest inhibition was obtained for the major matrix-associated proteoglycans, versican, decorin, and the **large heparan sulfate proteoglycans**, with synthesis values reduced by between 60 and 70%. Biglycan and other heparan sulfate proteoglycans were also affected, with synthesis values reduced by between 25 and 45%. In contrast, total protein synthesis was unaffected. Furthermore, effects of **cadmium** at the protein level were mirrored by reduction in messenger RNA levels for alpha1(I) procollagen, versican, and decorin. **These data support the hypothesis that cadmium may play an important role in the**

pathogenesis of emphysema associated with chronic inhalation of cadmium fumes by inhibiting the production of connective tissue proteins.

The following study indicates that copper protects cells from cadmium toxicity.

Title

Protective effect of copper against cadmium cytotoxicity on cultured vascular endothelial cells.

Author

Kaji T; Fujiwara Y; Koyanagi E; Yamamoto C; Mishima A; Sakamoto M; Kozuka H

Address

Department of Environmental Science, Faculty of Pharmaceutical Sciences, Hokuriku University, Kanazawa, Japan.

Source

Toxicol Lett, 63(1):13-20 1992 Oct

Abstract

We investigated the effect of copper on **cadmium**-induced cytotoxicity on vascular endothelial cells from bovine aorta in a culture system. Cytotoxicity was evaluated by the [³H]adenine release assay and the histological observation. After a 24-h incubation, **cadmium** exhibited a significant cytotoxicity on confluent cultures of endothelial cells in a dose-dependent manner, while copper only slightly did after a 24-h incubation. It was found that copper (5 microM) significantly decreased **cadmium** (1 and 2 microM) cytotoxicity; histologically, formation of de-endothelialized areas in the cell layer caused by **cadmium** was reduced by copper. The accumulation of **cadmium** in the cell layer was significantly decreased by copper; however, that of copper was unaffected by **cadmium**. **It was therefore suggested that copper significantly protects cadmium-induced cytotoxicity on cultured endothelial cells primarily through decreasing the cellular cadmium accumulation.**

The following study is significant because it shows that alcohol increases cadmium uptake into the body and have a combined stronger effect in decreasing copper and zinc levels. This demonstrates the danger of combined smoking and drinking in damaging the thyroid.

Title

Effect of ethanol on cadmium uptake and metabolism of zinc and copper in rats exposed to cadmium.

Author

Sharma G; Sandhir R; Nath R; Gill K

Address

Department of Biochemistry, Postgraduate Institute, Medical Education and Research, Chandigarh, India.

Source

J Nutr, 121(1):87-91 1991 Jan

Abstract

Effects of chronic administration of **cadmium** and ethanol, alone as well as in combination, on the **uptake of cadmium and its interaction with other essential trace elements** in various tissues of adult rats were investigated. **Cadmium given in combination with ethanol led to a pronounced increase in cadmium absorption and accumulation** in all the tissues studied relative to both non-exposed controls and rats treated with **cadmium** alone. **Both cadmium and ethanol exhibited specific effects on copper and zinc levels of the tissues.** These effects often were significantly altered when the animals were co-exposed to **cadmium** and ethanol. **The results suggested that although both cadmium and ethanol individually pose a hazard to essential trace metal homeostasis of various organs, co-exposure can pose a major threat since animals exposed to ethanol absorb much more cadmium than their unexposed counterparts.**

The following study suggests that the mechanism by which cadmium antagonizes zinc may be from its ability to substitute for zinc in the zinc finger DNA binding domain and this may be the way cadmium causes toxicity and cancer.

Title

Effect of replacement of "zinc finger zinc" on estrogen receptor DNA interactions.

Author

Predki PF; Sarkar B

Address

Department of Biochemistry Research, Hospital for Sick Children, Toronto, Ontario, Canada.

Source

J Biol Chem, 267(9):5842-6 1992 Mar 25

Abstract

Exposure of bovine estrogen receptor to the metal chelators EDTA and 1,10-phenanthroline results in a loss of nonspecific DNA binding, presumably because of the removal of "zinc finger zinc." Nonspecific DNA binding, as measured by a DNA-cellulose binding assay, can be restored by dialysis of the aporeceptor against buffer containing zinc, **cadmium**, and cobalt but not with buffer containing copper or nickel. More detailed studies were carried out using a bacterially expressed polypeptide encompassing the DNA binding domain of the human estrogen receptor. Apopolypeptide fails to bind DNA specifically, as measured by mobility shift assay using a consensus estrogen response element hexamer containing oligonucleotide, but DNA binding was restored by dialysis of the apopolypeptide against buffer containing zinc, **cadmium**, and cobalt but not with buffer containing copper or nickel. Dissociation constants of zinc- and **cadmium**-reconstituted polypeptide for the estrogen response element hexamer (66 and 48 nM, respectively) are virtually indistinguishable from native polypeptide (K_d = 48 nM) whereas cobalt-reconstituted polypeptide has a lower affinity (K_d = 720 nM). However, native, zinc-, **cadmium**-, and cobalt-reconstituted polypeptides gave identical results in a methylation interference assay. Competition experiments with zinc and copper or nickel suggest that copper and nickel are able to bind to zinc finger residues but do so nonproductively. The relative affinities copper greater than **cadmium** greater than zinc greater than cobalt greater than nickel for the polypeptide were determined by a zinc blot competition assay. **The ability of cadmium and cobalt to substitute for zinc in the zinc fingers demonstrates a structural "flexibility in the DNA binding domain as each of these metals has slightly different ionic radii. On the other hand, subtle differences in DNA binding affinity and/or specificity could exist, which may not be detectable here. Also, the ability of metals to substitute for zinc in the DNA binding domain suggests that metal substitution in these zinc fingers in vivo may be of relevance to the toxicity and/or carcinogenicity of some of these metals.**

The following study shows that cadmium damages the cells of the thyroid, reduces thyroglobulin producing cells, and decreases both T4 and T3.

Title

Cadmium toxicity in the thyroid gland of pregnant rats.

Author

Yoshizuka M; Mori N; Hamasaki K; Tanaka I; Yokoyama M; Hara K; Doi Y; Umezu Y; Araki H; Sakamoto Y; et al

Address

Department of Anatomy, School of Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan.

Source

Exp Mol Pathol, 55(1):97-104 1991 Aug

Abstract

The toxic effects of **cadmium** on the thyroid gland of pregnant rats were studied with an electron microscope and an X-ray microanalyzer. Serum levels of thyroid hormones (T3 and T4) were also analyzed. **Deterioration of the rough-surfaced endoplasmic reticulum occurred in the thyroid follicular epithelium on the fifth day of cadmium treatment.** Large intracellular vacuoles, which arose from dilated cisternae of the rough-surfaced endoplasmic reticulum, were fused together, and **marked swelling of the mitochondria** was also noted. **Thyroglobulin-secreting granules at the apical cytoplasm were decreased in number.** By energy dispersive X-ray microanalysis, **cadmium** peaks were preferentially obtained from swollen mitochondria in the follicular epithelial cells. **Serum levels of T3 and T4 were significantly decreased in cadmium-treated rats dams when compared to those of controls.** In the present experiment, cycloheximide also caused degenerative changes in the rough-surfaced endoplasmic reticulum and the disappearance of thyroglobulin-secreting granules. Cycloheximide is a known inhibitor of protein synthesis on cytosolic ribosomes. **These results indicated that accumulated cadmium in the mitochondria of thyroid follicular epithelial cells might disturb the oxidative phosphorylation of this organelle and the loss of energy supply possibly caused the inhibition of the synthesis and release of thyroid hormones.**

The following study shows that cadmium decreases T3, probably by inhibiting hepatic 5'-monodeiodinase (5'D-I) activity, which is a selenium dependent function. Cadmium is a known selenium antagonist while vitamin E facilitates selenium metabolism. Vitamin E was shown to protect against cadmium toxicity and maintain 5'D-I activity and T3 levels. While the experimenters concluded that "the metal-induced inhibition in hepatic 5'D-I activity is mediated through LPO (lipid peroxidation)" my conclusion is that the cadmium inhibited 5'D-I activity by decreasing selenium. While vitamin E does decrease lipid peroxidation, it does this by facilitating selenium metabolism and selenium is the key metal in glutathione peroxidase which is a potent inhibitor of lipid peroxidation.

Title**Title**

Cadmium induced thyroid dysfunction in chicken: hepatic type I iodothyronine 5'-monodeiodinase activity and role of lipid peroxidation.

Author

Gupta P; Kar A

Address

Thyroid Research Unit, School of Life Sciences, D.A. University, Vigyan Bhawan, Indore, India.

Source

Comp Biochem Physiol C Pharmacol Toxicol Endocrinol, 123(1):39-44 1999 May

Abstract

Administration of cadmium chloride (2.5 mg/kg body weight/day) to chickens daily for 15 days decreased serum triiodothyronine (T3) concentration (by 68.75%) without altering the levels of serum thyroxine (T4). Hepatic 5'-monodeiodinase (5'D-I) and superoxide dismutase (SOD) activities were also decreased (by 90.47% and 20.81% respectively) with a concomitant increase in lipid peroxidation (LPO, by 206.25%). Administration of the antioxidant vitamin E (alpha-tocopherol, 5 mg/kg body weight on alternate days) to cadmium intoxicated chickens restored thyroid function by maintaining normal hepatic 5'D-I activity and serum thyroid hormone concentrations. It also prevented **cadmium**-induced increase in LPO. We conclude that the metal-induced inhibition in hepatic 5'D-I activity is mediated through LPO.

The following study shows that vitamin C (ascorbic acid, AA) can prevent the decrease in 5'D-I activity caused by cadmium and thereby maintain T3 levels, but it can't restore T4 levels.

Title**Title**

Role of ascorbic acid in **cadmium**-induced thyroid dysfunction and lipid peroxidation.

Author

Gupta P; Kar A

Address

Thyroid Research Unit, School of Life Sciences, Devi Ahilya University, Indore, India.

Source

J Appl Toxicol, 18(5):317-20 1998 Sep-Oct

Abstract

A study on the effects of ascorbic acid (AA) on heavy metal (cadmium)-induced thyroid dysfunction and lipid peroxidation (LPO) was carried out in Swiss male mice. The animals were administered with either **cadmium** (1.0 mg kg⁻¹ body wt.) alone or in combination with AA (1 mM) every day for 15 days. While **cadmium** treatment led to a decrease in the serum concentrations of thyroid hormones and hepatic type I iodothyronine 5'-monodeiodinase (5'D-I) activity, an increase in the level of lipid peroxidation was observed. **The metal-induced decrease in hepatic 5'D-I activity and serum triiodothyronine (T3) concentration was restored by treatment with AA. However, AA could not restore the serum thyroxine (T4) concentration.** The increased level of LPO was also ameliorated by AA. It appears that the protective effect of AA against **cadmium**-induced thyroid dysfunction is mediated through its antioxidative action.

The following study, while it has no abstract, indicates that testosterone reduces the cadmium induced inhibition of thyroid function. Other studies indicate that testosterone facilitates cadmium excretion from the body. This is another indication that there are sex differences in cadmium induced inhibition of thyroid function.

Title**Title**

Role of testosterone in ameliorating the **cadmium** induced inhibition of thyroid function in adult male mouse.

Author

Gupta P; Kar A

Address

Thyroid Research Unit, School of Life Sciences, Devi Ahilya University, Vigyan Bhawan, Khandwa Road Campus, Indore 452 001, India.

Source

Bull Environ Contam Toxicol, 58(3):422-8 1997 Mar

The significance of the following study is that in addition to showing that cadmium decreases both T4 and T3, cadmium prevents TSH from rising to correct the low T4 and T3 problem. This means that in our era when doctors test only TSH to determine thyroidal function, many people have undetected low thyroid function. This is a very important finding since we see so many people with problems of low energy and weight gain, but their doctors are telling them their thyroid function is normal. This one study demonstrates the extreme importance of testing T4 and T3 and not just TSH.

Title

Evidence suggesting that cadmium induces a non-thyroidal illness syndrome in the rat.

Author

Pavia J'union MA; Paier B; Noli MI; Hagm"uller K; Zaninovich AA

Address

CONICET, Hospital de Cl'nicas, University of Buenos Aires, Argentina.

Source

J Endocrinol, 154(1):113-7 1997 Jul

Abstract

The effect of in vivo administration of *cadmium* chloride on the pituitary-thyroidal axis was assessed in 200 g body weight Wistar rats. A dose of 2.5 mg/kg body weight was injected i.v. 24 h before the experiments were initiated. **Plasma thyroxine (T4) and tri-iodothyronine (T3) concentrations in cadmium-treated rats were significantly ($P < 0.01$) decreased, whereas plasma TSH failed to increase in response to low T4 and T3.** However, the TSH response to TRH and the pituitary content of TSH in these rats were both normal. *Cadmium* induced a significant ($P < 0.01$) decrease in 4-h thyroidal ¹³¹I uptake and in thyroid/plasma radioactivity ratio. **The in vitro conversion of T4 to T3 in the pituitary was significantly ($P < 0.01$) blocked by cadmium** whereas there was no in vivo effect. Parameters of peripheral T4 kinetics in *cadmium*-treated rats, such as metabolic clearance rate ($P < 0.01$), fractional turnover rate ($P < 0.01$), absolute disposal rate ($P < 0.05$), urinary clearance ($P < 0.05$) and faecal clearance ($P < 0.05$), were all decreased by *cadmium*. **The lack of response of TSH to low plasma T4 and T3 and the normal response to exogenous TRH in this and in other non-thyroidal illness syndromes produced by other pathologies suggest a decreased stimulation of pituitary thyrotrophs by endogenous TRH.**

The following study might indicate that thyroid hormones are essential to repair the damage caused by cadmium. This mechanism might explain why ophthalmopathy increases in RAI treated humans.

Title

***Cadmium*-induced acute lung injury: compromised repair response following thyroidectomy.**

Author

Palmer KC; Mari F; Malian MS

Source

Environ Res, 41(2):568-84 1986 Dec

Abstract

The role of thyroid hormone in the pulmonary repair process following cadmium chloride-induced acute injury, was assessed in the present study. Thyroidectomized (Thyx), male Sprague-Dawley rats were exposed by inhalation to *cadmium* chloride aerosol (CdCl₂, 10 mg/m³). Rats were sacrificed 1 hr after [³H]thymidine (3H-T) injection at intervals up to 10 days after exposure. Thyroidectomy, followed by CdCl₂, produced earlier and more severe acute injury in the form of alveolar hemorrhage edema and hyaline membrane formation, than CdCl₂ alone. However, Type 2 cell hyperplasia was markedly reduced in this group of rats compared with CdCl₂ controls. Uptake of 3H-T by Thyx-CdCl₂ lung tissue was only 40% of that measured in CdCl₂ controls. Autoradiographic studies indicated that Type 2 cell labeling was less than 66% of controls up to 3 days after exposure. Cells obtained by lung lavage of Thyx-CdCl₂ rats were reduced in number up to 60% with respect to controls, during the first week after exposure. Additionally, the activities of lung antioxidant enzymes (glucose-6-phosphate dehydrogenase, superoxide dismutase, and glutathione peroxidase) were significantly inhibited (45-55%) throughout the experiment in Thyx-CdCl₂ animals compared with normal rats. In summary, thyroidectomy impairs the repair response in CdCl₂ lung damage by enhancing Type 2 cell damage, reducing Type 2 cell proliferation, altering alveolar macrophage populations, and depressing antioxidant defense systems.

The following study demonstrates the presence of cadmium-binding proteins (CdBPs) present in humans in the kidney, liver, pancreas, and thyroid gland, offering evidence that could be interpreted that cadmium is an essential nutrient since the body has specific proteins to transport it.

Title

Cadmium-binding proteins in human organs.

Author

Sato M; Takizawa Y

Source

Abstract

Cadmium-binding proteins (CdBPs) in the cytosol fractions from several organs of man orally exposed to cadmium (Cd) were examined by gel chromatography. In kidney and liver most of the cadmium (76-87%) in the cytosols was bound to metallothionein, and hepatic metallothionein contained zinc also at a similar level. The pancreas cytosol also contained a metallothionein-like CdBP, although its content was only one-tenth of the hepatic one. In the thyroid gland a prominent CdBP, eluting later than that of metallothionein, was observed; this CdBP was not detectable in normal dogs, pigs, and oxen. No CdBPs were observed in other organs including heart, muscle, genital organs, aorta, and bone. These results suggest that CdBPs participate in accumulation and distribution of cadmium in man, since organs containing CdBP such as kidney, liver, pancreas, and thyroid gland show a tendency to accumulate high levels of cadmium.

The following study shows that testosterone pretreatment protects certain species, but not all species, from cadmium toxicity. The method of protection is hypothesized to be increased production of metallothionein, a protein that transports metals including cadmium and zinc.

Title

Testosterone pretreatment mitigates **cadmium** toxicity in male C57 mice but not in C3H mice.

Author

Shimada H; Bare RM; Hochadel JF; Waalkes MP

Address

Laboratory of Comparative Carcinogenesis, National Cancer Institute, Frederick Cancer Research and Development Center, MD 21702-1201, USA.

Source

Toxicology, 116(1-3):183-91 1997 Jan 15

Abstract

Previous work has indicated that testosterone pretreatment protects against cadmium-induced toxicity in male rats while other data indicate that pretreatment of mice with testosterone offers no such protection against cadmium. Since cadmium toxicity may vary widely with species and strain, we examined the effect of testosterone pretreatment on cadmium toxicity in two strains of mice, one that is sensitive (C3H) and one that is resistant (C57) to cadmium toxicity. A single sc injection of 20 micromol CdCl₂/kg to C3H mice or 45 micromol CdCl₂/kg to C57 mice proved very toxic, causing 50%, and 44% mortalities, respectively. However, when C57 mice were pretreated with testosterone (5 mg/kg, s.c., at - 48, - 24, and 0 h) prior to cadmium (45 micromol/kg), complete resistance to cadmium-induced lethality developed. Testosterone had no effect on cadmium-induced lethality in C3H mice. Testosterone prevented extensive hepatocellular damage caused by cadmium in C57 mice and also significantly reduced cadmium-induced elevations in serum lactate dehydrogenase (LDH) activity and blood urea nitrogen (BUN), which are indicators of hepatic and renal function, respectively. The toxicokinetics of cadmium were apparently not affected by testosterone pretreatment, as the distribution of cadmium to liver in either strain was unchanged by the steroid. Cadmium-induced metallothionein (MT) levels in liver and kidney of C57 mice were increased in testosterone-pretreated mice given the higher doses of metal but no such enhancement of MT synthesis occurred in C3H mice. This increase in MT may provide some level of protection against cadmium toxicity in the C57 mice. These results indicate that testosterone pretreatment prevents toxicity of cadmium in male C57 mice, possibly through enhancement of MT synthesis, but has no effect in male C3H mice.

Testosterone protects the body from cadmium toxicity. This study shows that cadmium in turn decreases testosterone. Since cadmium is a zinc antagonist and zinc is essential for the formation of testosterone, cadmium may decrease testosterone production by zinc reduction.

This effect suggests interesting hypotheses about why people smoke. Perhaps people smoke to reduce testosterone and become more relaxed, since testosterone is a known activity stimulant. Women might reduce their testosterone by smoking and "feel more feminine". Just speculation, of course.

Unfortunately, taking up smoking has serious long-term health consequences such as increased testicular cancer in men and increased thyroid disease in women.

Title

The effects of continuous testosterone exposure on spontaneous and **cadmium**-induced tumors in the male Fischer (F344/NCr) rat: loss of testicular response.

Author

Waalkes MP; Rehm S; Devor DE

Address

Inorganic Carcinogenesis Section, Laboratory of Comparative Carcinogenesis, Division of Basic Sciences, National Cancer Institute, Frederick Cancer Research and Development Center, Maryland 21702-1201, USA.

Source

Toxicol Appl Pharmacol, 142(1):40-6 1997 Jan

Abstract

In the rodent testes, cadmium induces severe necrosis followed by chronic degeneration. Cadmium is also an effective testicular tumorigen, and a single dose produces a high incidence of Leydig cell tumors. The mechanism of tumor formation is unknown, but pituitary feedback, i.e., increased luteinizing hormone (LH) production due to low circulating androgen, has been implicated in causation of proliferative lesions

within degenerate, hypofunctioning testes. Thus, the effects of androgen replacement on the testicular toxicity of **cadmium** in Fischer (F344/NCr) rats was studied. Groups (n = 50) of 10-week-old rats either received testosterone implants that approximate normal circulating levels in castrated rats or were left untreated. After 2 weeks of stabilization, rats were given either 20 micromol CdCl₂/kg, s.c., weekly for the next 5 weeks (total dose 100 micromol/kg) or saline for a total of four treatment groups (control, testosterone alone, testosterone + **cadmium**, or **cadmium** alone). Portions of each group were killed either 10 weeks after initiation of **cadmium** exposure (n = 10), for assessment of endocrine function, or over the next 2 years (n = 40), for assessment of testicular neoplastic lesions. **At 10 weeks, cadmium reduced circulating testosterone in nonimplanted rats by nearly 80% and induced a marked weight loss of the testes (>70%) and sex accessory glands (reflected in a 50% reduction in prostate mass). Testosterone implantation restored circulating testosterone levels in cadmium-treated rats and prevented Cd-induced weight loss of the sex accessory glands but not of the testes.** Over 2 years, **cadmium** alone induced a >84% incidence of Leydig cell neoplasia and a >97% incidence of chronic degeneration, both significant increases over control rates (60 and 0%, respectively). Testosterone implantation abolished both **cadmium**-induced and spontaneously occurring Leydig cell tumors but had no effect on **cadmium**-induced chronic testicular degeneration. **Thus cadmium-induced hypofunction of the testes, and subsequent loss of circulating testosterone, appears to be a critical aspect in cadmium induction of tumors in the rat testes.**

The following study demonstrates that estradiol (estrogen) causes a more rapid uptake of cadmium by the liver and also an enhanced induction of metallothionein (MT) in both the liver and kidney. This is very good evidence that women are going to have greater cadmium accumulation and this may be the mechanism by which women have a greater incidence of thyroid disease than men. The question remaining is why does estradiol increase cadmium accumulation? Is it just a by-product of metallothionein production? Increased metallothionein production would be beneficial for females because it increases the storage of trace elements such as zinc which are needed for pregnancy. Perhaps the problem is that our industrialized society has significantly increased concentrations of cadmium. Then estradiol causes the inadvertent accumulation of cadmium into female bodies because of this increased concentration in our environment.

Title

Sex differences in hepatic and renal **cadmium** accumulation and metallothionein induction. Role of estradiol.

Author

Blazka ME; Shaikh ZA

Address

Department of Pharmacology and Toxicology, University of Rhode Island, Kingston 02881.

Source

Biochem Pharmacol, 41(5):775-80 1991 Mar 1

Abstract

The role of estradiol in sex differences in hepatic and renal cadmium accumulation and metallothionein (MT) induction was investigated. Male and female rats and castrated males pretreated with estradiol were injected either i.v. or s.c. with 10 mumol CdCl₂/kg. Sex differences in **cadmium** accumulation and MT induction were apparent after s.c. but not i.v. administration. **The female rats accumulated a significantly greater concentration of cadmium in their liver than did the males, as early as 1 hr after the s.c. injection.** The elevated levels of **cadmium** in the females were maintained for at least 10 days. **Pretreatment of castrated males with estradiol caused a similarly greater accumulation of cadmium in the liver.** Hepatic MT levels peaked in the females at 24 hr and in males 48-72 hr after the **cadmium** injection and then declined to lower levels. This superinduction of MT occurred only after the s.c. administration of **cadmium**. MT levels in both sexes plateaued 5 days after the s.c. injection to the levels that were similar to those seen in male and female rats 24 hr after an i.v. injection. In animals injected s.c. with **cadmium** the renal **cadmium** levels continued to rise for 5-10 days; however, in animals injected i.v. the levels stabilized within 2 hr. The renal MT levels in the females were significantly higher than in the males. **Estradiol pretreatment induced renal MT but did not affect renal cadmium accumulation.** Thus, the sex differences in hepatic **cadmium** accumulation and MT induction are affected by the route and time after the administration of **cadmium**. **Furthermore, estradiol causes a more rapid uptake of cadmium by the liver and also an enhanced induction of MT in both the liver and kidney.**

In contrast to the prior study, these researchers conclude that estradiol increases the accumulation of cadmium without inducing the synthesis of metallothionein. However, they agree that estradiol does increase the accumulation of cadmium.

Title

Stimulation of **cadmium** uptake by estradiol in the kidney of male rats treated with **cadmium**.

Author

Nishiyama S; Onosaka S; Taguchi T; Konishi Y; Tanaka K; Kinebuchi H

Address

Department of Environmental and Occupational Health, Kochi Medical School, Japan.

Source

Biochem Pharmacol, 37(16):3091-6 1988 Aug 15

Abstract

The present study was carried out to analyze the sex differences in the retention of Cd in rats treated with a small amount of Cd, and its mechanisms. Cd and Zn concentrations in the kidney and liver of female rats treated with 28 nmol Cd or 1 nmole Zn were significantly higher than those in male rats. Pretreatment with estradiol (1.8 mumol/kg of b.w., twice a day, 6 consecutive days) increased the Cd and Zn concentrations in the kidney of male rats treated with Cd or Zn. Incubation of MDCK cells with 10(-5) M estradiol, 10(-5) M

stilboestrol and 10(-5) M progesterone caused a significant increase in Cd uptake. These results suggest that endogenous female sex hormones may play a role in a higher concentration of Cd and Zn in the kidney of female rats than that in male rats. The basal level of metallothionein (MT) in the liver and kidney of control female rats was within the same range as that in the control male rats. Cd and Zn accumulations caused by pretreatment with estradiol in the kidney of male rats treated with Cd or Zn were so low (Cd: 38 ppb, Zn: 1.0 ppb) as to be probably unable to induce the synthesis of MT. An increase in the concentration of Cd in the cultured renal cells occurred 1 hr after treatment with estradiol and Cd. Pretreatment with estradiol alone also resulted in a modification of the concentration of Na and K, which cannot be bound to MT. **Together, all of the above findings suggest that estradiol directly increases the accumulation of Cd into the renal cells without inducing the synthesis of MT.**

The following study shows that in a population of women, cadmium concentrations increase with age and the cadmium/zinc ratio increases with age indicating that zinc does not increase in proportion to cadmium. This declining zinc/cadmium ratio could be an explanation for increased incidence of hypothyroidism with age.

Title

Cadmium and zinc concentrations in human placentas.

Author

Fiala J; Hrub'a D; R'ezl P

Address

Institute of Preventive Medicine, Faculty of Medicine, Masaryk University, Brno, Czech Republic.

Source

Cent Eur J Public Health, 6(3):241-8 1998 Aug

Abstract

Cadmium and zinc levels in placentae of 688 women who delivered their children in two university hospitals in Brno and in the regional hospital in Znojmo during January-June 1992 were determined using AAS analytical method. Average value of zinc (54.6 micrograms/g) and **cadmium** (18.02 ng/g) concentrations found out in our file are in accord with those ones reported in literature. Individual differences in zinc contained in placentae occur uniformly. Very low concentrations prevail for **cadmium**; values exceeding 100 ng/g of dry basis are sporadic only. Zinc vs. **cadmium** concentrations values in placenta are mutually positively correlated [correlation coefficient (factor) $r = +0.13$, $p < 0.001$]. **Cadmium content in placenta depends on mothers' age and it is significantly higher in older women.** No changes in zinc contained in the placental tissue depending on mothers' age were found out. **The mutual ratio of zinc vs. cadmium content in a placental tissue is significantly decreased in older mother (23.8 in older women, 41.2 in younger women, $p < 0.01$).**

The following study clearly indicates that cadmium is associated with and probably causes bone demineralization, decreased bone density in women, and decreased height in men. People living downwind of zinc smelters face increased dangers because cadmium and zinc are found in the same ore. Since all industrialized areas have increased amounts of air-, water-, and food-borne cadmium, everyone is at risk for cadmium toxicity and resultant osteoporosis.

Title

Environmental exposure to **cadmium**, forearm bone density, and risk of fractures: prospective population study. Public Health and Environmental Exposure to **Cadmium** (PheeCad) Study Group.

Author

Staessen JA; Roels HA; Emelianov D; Kuznetsova T; Thijs L; Vangronsveld J; Fagard R

Address

The Hypertensie en Cardiovasculaire Revalidatie Eenheid, Departement Moleculair en Cardiovasculair Onderzoek, Katholieke Universiteit Leuven, Belgium. jan.staessen@med.kuleuven.ac.be

Source

Lancet, 353(9159):1140-4 1999 Apr 3

Abstract

BACKGROUND: Chronic low-level exposure to cadmium may promote calcium loss via urinary excretion. We undertook a prospective population study to investigate whether environmental exposure to cadmium lowers bone density and increases risk of fractures. **METHODS:** We measured urinary **cadmium** excretion, a biomarker of lifetime exposure, in people from ten districts of Belgium, of which six districts bordered on three zinc smelters. We also measured **cadmium** in soil and in vegetables from the districts, and collected data on incidence of fractures and height loss. Bone density was measured at the forearm just above the wrist by single photon absorptiometry, and calculated as the mean of six proximal and four distal scans. **FINDINGS:** Mean **cadmium** excretion at baseline was 8.7 nmol daily. Across the ten districts, mean **cadmium** concentration in soil ranged from 0.8 to 14.7 mg/kg, and from 0.1 to 4.0 mg/kg dry weight in vegetables. Median follow-up was 6.6 years. Mean forearm bone density in proximal and distal scans was 0.54 g/cm² and 0.43 g/cm² in men, and 0.44 g/cm² and 0.34 g/cm² in women. **In postmenopausal women, a twofold increase in urinary cadmium correlated with 0.01 g/cm² decrease in bone density ($p < 0.02$). The relative risks associated with doubled urinary cadmium were 1.73 (95% CI 1.16-2.57; $p = 0.007$) for fractures in women and 1.60 (0.94-2.72, $p = 0.08$) for height loss in men. Cadmium excretion in districts near smelters was 22.8% higher ($p = 0.001$) than in other districts, with fracture rates of 16.0 and 10.3 cases per 1000 person-years, respectively, and a population-attributable risk of 35.0%.** **INTERPRETATION: Even at a low degree of environmental exposure, cadmium may promote skeletal demineralisation, which may lead to increased bone fragility and raised risk of fractures.**

The following study supports the hypothesis that cadmium toxicity effects are mediated by decreases in

selenium and glutathione peroxidase (a selenium-based antioxidant). Also noted, and this may be very important, is that cadmium causes copper, zinc, and manganese to transfer out of the mitochondria of cells. Other evidence suggests that a copper deficiency in the mitochondria is a factor in the genesis of hyperthyroidism.

Title [Changes in trace elements contents of renal cells in **cadmium** poisoning]

Author

Long M; Zhao J; Wang S

Address

Department of Preventive Medicine, Guiyang Medical College, Guizhou.

Source

Chung Hua Yu Fang I Hsueh Tsa Chih, 32(2):73-5 1998 Mar

Abstract

OBJECTIVE: To understand the possible role of trace elements in renal damage caused by **cadmium** poisoning and its mechanism. **METHODS:** An experimental animal model with renal damage caused by **cadmium** poisoning was prepared, and trace elements contents in subcellular components in renal cells, lipid peroxidation reaction, renal function and its ultrastructural changes were determined. **RESULTS: Uptake of cadmium could cause transfer of copper, zinc and manganese mainly distributed in the mitochondrion to cell nuclei and cytoplasm, and content of selenium and activity of glutathione-peroxidase (GSH-px) in cytosol declined and content of propandiolal increased.** **CONCLUSION: It suggests that changes in trace elements contents, especially in selenium content, during renal damage caused by cadmium poisoning, could correlate with the increase of lipid peroxidation, and abnormal subcellular distribution of trace elements was one of the important roles in renal damage caused by cadmium poisoning.**

The following study demonstrates that fasting or interrupting the nutrient supply decreases the body's resistance to cadmium toxicity.

Title

Effects of fasting on **cadmium** toxicity, glutathione metabolism, and metallothionein synthesis in rats.

Author

Shimizu M; Morita S

Address

Department of Environmental Health, Osaka City Institute of Public Health and Environmental Sciences, Japan.

Source

Toxicol Appl Pharmacol, 103(1):28-39 1990 Mar 15

Abstract

Acute oral toxicity of Cd (as cadmium chloride) was enhanced in rats fasted 24 hr, as shown by a markedly decreased LD50. To examine the relationship among Cd toxicity, hepatic glutathione (GSH), and metallothionein (MT) during fasting, rats were administered 75 mg Cd/kg orally 24 hr after fasting and euthanized after a further 4 or 24 hr for various assays. Serum glutamic-pyruvic transaminase activity 24 hr after Cd treatment was higher in fasted rats than in fed rats. Both total GSH and nonprotein sulfhydryl (NPSH) concentrations in liver decreased to 50% of control levels after 28 hr of fasting and returned to 75% of control values by 48 hr. Total hepatic GSH concentration in fed rats decreased 4 and 24 hr after Cd treatment, whereas that in fasted rats remained unchanged at 4 hr and decreased significantly at 24 hr. Cd uptake by the liver (both concentration and content) 24 hr after Cd treatment was higher in fasted rats than in fed rats. Hepatic MT concentration was markedly increased by Cd treatment and higher in fasted rats than in fed rats. There was no relationship between Cd toxicity and hepatic thiobarbituric acid (TBA) value, an indicator of lipid peroxidation. Fasting had no effect on hepatic GSH peroxidase and GSH reductase activities. These enzymes probably are not involved in Cd toxicity. On histological examination, focal degenerative and necrotic changes were observed from the midlobular to the pericentral region in the livers of fed rats 24 hr after Cd treatment. These changes were enhanced by fasting, diffusing from the pericentral to the periportal region. Histochemical examination revealed a heterogeneous distribution of GSH in the livers of fed rats, with strong staining of GSH in the periportal region. This heterogeneous distribution of GSH in liver was not observed in fed rats 4 hr after Cd treatment or in fasted rats at 24 hr. **The present results suggest that hepatic GSH plays an important role in protection against Cd toxicity before the onset of MT synthesis. Animals in bad condition, such as that resulting from interruption of nutrient supply, cannot be protected against Cd toxicity even if the hepatic MT level is high.**

The following study indicates that vitamin C (ascorbic acid) protects against cadmium toxicity without inducing metallothionein production.

Title

Effect of L-ascorbic acid pretreatment on **cadmium** toxicity in the male Fischer (F344/NCr) rat.

Author

Shiraishi N; Uno H; Waalkes MP

Address

Inorganic Carcinogenesis Section, National Cancer Institute, Frederick Cancer Research and Development Center, MD 21702-1201.

Source

Toxicology, 85(2-3):85-100 1993 Dec 31

Abstract

Some studies have indicated that cadmium-induced lethality and selective injurious effects to specific tissues, such as testes or liver, can be prevented by pretreatment with the antioxidant L-ascorbic acid

(**ascorbic acid**). However, the basis of this tolerance is unclear. We examined the effects of ascorbic acid pretreatment on **cadmium** toxicity in male Fischer (F344/NCr) rats. **Cadmium** treatment alone (25 $\mu\text{mol CdCl}_2/\text{kg}$, s.c.) proved lethal, causing a 93% mortality within 72 h, but in rats pretreated with ascorbic acid (2 g/kg, s.c. 24, 12 and 1 h) **cadmium**-induced lethality was nearly prevented. Hepatic lesions, including hepatocellular necrosis, induced by **cadmium** were at least partially ameliorated by ascorbic acid pretreatment. Ascorbic acid pretreatment had no effect on **cadmium**-induced testicular lesions nor on **cadmium** content in testes, liver, kidney and urine. Ascorbic acid alone modestly increased hepatic metallothionein (MT), but not renal MT and had no effect on induction of hepatic or renal MT by **cadmium**. In contrast to liver and kidney, testicular **cadmium**-binding protein (TCBP) in rats exposed to **cadmium** alone decreased markedly. Moreover, the level of TCBP decreased unexpectedly in ascorbic acid pretreated rats as compared with control. **These results indicate that ascorbic acid pretreatment decreases the toxicity of cadmium in the rat without markedly modifying its toxicokinetics or markedly stimulating MT synthesis.**

The following two studies demonstrate the protective effect of selenium against cadmium toxicity.

Title

[The protective effect of simultaneous selenium administration on acute **cadmium** toxicity and metallothionein]

Author

Ohta H; Imamiya S; Yoshikawa H

Address

Department of Health Administration, School of Hygienic Sciences, Kitasato University.

Source

Sangyo Igaku, 30(6):451-8 1988 Nov

Abstract

The present study was conducted to elucidate the protective action of simultaneous selenium administration against acute cadmium toxicity. The remarkable testicular damages caused by cadmium, that is, hemorrhagic inflammation, atrophy and necrosis, were lessened by simultaneous selenium administration. Cadmium concentration in blood, especially in plasma, increased significantly during the early period after **cadmium** administration with selenium. **Cadmium** and selenium in plasma were found in the same fractions of high molecular weight reported by previous workers as the high molecular weight complex containing **cadmium** and selenium. **Cadmium** in testis was also noted in the high molecular weight fraction during the early period. However, **cadmium** in the high molecular weight fraction of plasma and testis were unstable and decreased rapidly by lapse in time. **Cadmium** concentration in liver was lower than that in the group administered **cadmium** alone during the increasing phase of plasma **cadmium**. However, in contrast with the decreased **cadmium** level in plasma, **cadmium** in liver and testis increased gradually. **Cadmium** increased in liver and testis were also found in the metallothionein fraction. In the testis protected from acute **cadmium** toxicity, the inhibitory effect of glutathione S-transferase activity by **cadmium** was not detectable and the activity was maintained at the level of the control (saline administered group). Moreover, the increased **cadmium** in the metallothionein fraction was related to the decrease of **cadmium** in the high molecular weight fraction of the testis homogenate. In addition, a positive correlation was observed between metallothionein concentration and glutathione S-transferase activity.(ABSTRACT TRUNCATED AT 250 WORDS)

Biometals 1999 Dec;12(4):353-9

Cadmium induced lipid peroxidation in rat testes and protection by selenium.

Yiin SJ, Chern CL, Sheu JY, Lin TH

Graduate Institute of Medicine, Kaohsiung Medical University, Taiwan.

[Medline record in process]

The main goal of this study was to investigate the role of cadmium in the promotion of lipid peroxidation in the homogenates of rat testes and the effect of selenium on lipid peroxidation in testes of rats after cadmium injection. Treatment of rats with cadmium resulted in a time- and dose-related accumulation of the metal ions in testes. The concentrations of cadmium, copper, zinc, selenium and iron in the tissues were determined by an atomic absorption spectrophotometer and lipid peroxidation in testes was measured by a spectrophotometer. Cadmium produced enhanced lipid peroxidation in testes. These cadmium-induced changes were accompanied by a significant increase of iron and copper, and a decrease of zinc in testes. Concurrent treatment with selenium and cadmium reduced the cadmium-induced alterations in lipid peroxidation and essential metal levels. **Data suggest that lipid peroxidation was associated with cadmium toxicity in testes and that the addition of selenium was found to be effective in attenuation of this effect.**

The following study demonstrates the protective effect of zinc against the toxicity of cadmium in preembryos.

Title

Zinc amelioration of **cadmium** toxicity on preimplantation mouse zygotes in vitro.

Author

Yu HS; Chan ST

Address

Department of Zoology, University of Hong Kong.

Source

Teratology, 37(1):13-9 1988 Jan

Abstract

Zinc, at a concentration of 5 or 10 micrograms/ml medium, has been shown to protect mouse preembryos in vitro from the toxicity of cadmium at a concentration of 5 micrograms/ml medium after a simultaneous treatment of the ions from four-cell to morula or from morula to blastocyst for 24 hours. Such an amelioration indicates that **cadmium** toxicity is a result of the unique property of the **cadmium** ion and is not due to an alteration in the culture medium after the addition of an extra metallic ion. Zinc probably ameliorates **cadmium**-treated mouse preembryo by competing with **cadmium** for uptake or some other metabolic processes. In view of the well-documented competition between **cadmium** and zinc ions for binding sites in many other cell types, some macromolecules to which similar divalent metallic ions bind competitively may also exist in the mouse preembryo. **This suggests that a protective mechanism dependent on the metal-metal interactions begins to operate in the mouse preembryo at a very early stage of differentiation before implantation.**

Following is a summary the health problems caused by cadmium and techniques for the removal of cadmium from the body. Particularly important is the statement that cadmium has a half-life of over 10 years in the body.

Title

Cadmium therapeutic agents.

Author

Kelley C

Address

Department of Chemistry, Northern Arizona University, Flagstaff, AZ 86011-5698,
USA.Colleen.Kelley@nau.edu

Source

Curr Pharm Des, 5(4):229-40 1999 Apr

Abstract

Pollution of the environment with toxic metals has increased dramatically since the beginning of the industrial revolution. **Cadmium is of particular concern because it accumulates in the human body with a half-life exceeding 10 years and has been linked with a number of health problems including renal tubular dysfunction, pulmonary emphysema, significant kidney damage, and possibly osteoporosis. Moreover, in 1993 the International Agency for Research on Cancer (IARC) classified cadmium and compounds containing cadmium as human carcinogens.** The field of **cadmium** intoxication therapy has seen increases in interest due to its poignant toxicity in both humans and animals. **Preliminary attempts to combat acute cadmium poisoning included the use of the chelating agents ethylenediaminetetraacetic acid (EDTA) and British anti-Lewisite (BAL).** This review will focus on the chemistry, biology, and effectiveness of **cadmium** intoxication therapy to date. The toxicokinetics of **cadmium** mammals will be discussed briefly to understand the extent and severity of overexposure. An overview of **cadmium** chelation therapy will be given with an emphasis on the measurable effectiveness of each and significant structure activity relationships. **Cadmium** intoxication therapy will be reviewed by their indicated routes of action: direct (chelation and antagonism), indirect (induction), and symptom alleviation. The methods by which **cadmium** therapeutics are evaluated (in vivo, in vitro) are to be discussed. An evaluation of the clinical potential for promising therapeutics will be given.

Here is a great study which shows that cadmium toxicity decreases blood levels of magnesium. We see that in Graves' disease there is evidence of cadmium toxicity and magnesium deficiency, manifested by increased heart rate, heart arrhythmias, and tremors. The connection fits with our observations.

Title

Contribution to interaction between magnesium and toxic metals: the effect of prolonged **cadmium** intoxication on magnesium metabolism in rabbits.

Author

Soldatović D; Matović V; Vujanović D; Stojanović Z

Address

Department of Toxicological Chemistry, Faculty of Pharmacy, University of Belgrade, Yugoslavia.

Source

Magnes Res, 11(4):283-8 1998 Dec

Abstract

The results obtained up to now indicate that increased intake of some heavy metals causes disorder of bioelements metabolism leading to their blood and organs decrease and higher elimination via the urine. **As to lead and magnesium, our investigations indicated that the reaction is reversible and that increased intake of Mg eliminates Pb via urine.** Some other findings suggest similar relations between Mg and certain heavy metals, thus pointing to significant role of Mg in toxicology of heavy metals and announcing a new chapter in the toxicology of metals entitled 'Mg in professional and ecotoxicology'. In this report we present the results of our investigations on the effect of Cd on Mg metabolism. The experiment was performed on rabbits given orally, every day, for 4 weeks 10 mg Cd/kg b.w. as aqueous solution of CdCl₂. Magnesium content was determined in blood, urine, soft tissues and bones by the AAS method. **Under the experimental conditions, Cd lead to statistically significant decrease of blood Mg (p < 0.001 after day 16) which was associated with increased Mg elimination via urine (p < 0.01).** Statistically significant changes were not detected in the tissues, except in the liver where we found enhanced Mg content (p < 0.05), while its level in the muscles decreased (p < 0.01).

As the following study indicates, cadmium has been implicated in the formation of cataracts in chronic smokers. This study shows that in addition to cadmium there is an accumulation of iron in the lens. Vitamin E is shown to protect the lens by blocking iron accumulation rather than blocking cadmium accumulation.

Title

Cadmium and iron accumulation in rat lens after cigarette smoke exposure and the effect of vitamin E (alpha-tocopherol) treatment.

Author

Avunduk AM; Yardimci S; Avunduk MC; Kurnaz L

Address

Karadeniz Technical University, School of Medicine, Department of Ophthalmology, Trabzon, Turkey.
avunduk@meds.ktu.edu.tr

Source

Curr Eye Res, 18(6):403-7 1999 Jun

Abstract

PURPOSE: Cadmium accumulation in the lens has been implicated in cataractogenesis of chronic smokers. This study was planned to evaluate whether or not in vivo cigarette smoke exposure causes cadmium accumulation in rat lens, and possible protective effect and mechanism of alpha-tocopherol (vitamin E) treatment on cataractogenesis. **METHODS:** 28 male Wistar rats were randomly divided into four equal groups. Group 3 and 4 rats were exposed to cigarette smoke over ninety consecutive days, and Group 1 and 2 rats were treated in a similar fashion but exposed only to room air. Additionally, vitamin E was given to Group 2 and 4 rats. **RESULTS:** Significantly higher iron levels were observed in the lenses of Group 3 rats compared to other groups. With respect to cadmium, Group 3 and 4 rats had significantly higher levels compared to Group 1 and 2 rats. Although vitamin E treatment prevented iron accumulation in Group 4 rats, it had no effect on cadmium concentrations. Distinct histopathological changes observed in Group 3 rats were not present in Group 4 rats. **CONCLUSION:** Our study demonstrates that in vivo cigarette smoke exposure causes accumulation of cadmium in rat lens and IM vitamin E treatment does not affect this accumulation. The protective effect of vitamin E treatment on smoke exposed rat lens seems to be mediated by blockage of iron accumulation in the lens.

The following study shows that cadmium causes decreases of selenium and calcium in the eye and increases of iron and copper in the eye when selenium levels are low. Copper accumulation in the eye is characteristic of certain copper accumulation diseases like Wilson's disease and schizophrenia. Perhaps the copper accumulates there because of low selenium and selenium supplementation might help those individuals' ability to metabolize copper properly.

Title

Cadmium-induced alterations in ocular trace elements. Influence of dietary selenium and copper.

Author

Jamall IS; Roque H

Address

Department of Health Services, Toxic Substances Control Division, Technical Services, Sacramento, CA 94234-7320.

Source

Biol Trace Elem Res, 23():55-63 1989-90 Winter

Abstract

The present report demonstrates, for the first time, that feeding rats 50 ppm cadmium for just 7 wk results in detectable levels of cadmium in the eye of rats. Furthermore, these ocular cadmium concentrations affect significant alterations in the levels of the essential trace elements selenium, calcium, iron, and copper in the eye. Rats were fed a low-selenium (less than 0.02 ppm selenium), high-copper basal diet (50 ppm copper) supplemented with 0, 0.1, and 0.5 ppm selenium. The animals were either untreated or treated with 50 ppm cadmium admixed with their feed. Cadmium treatment resulted in significant reductions (up to 50%) in ocular selenium. Furthermore, rats fed the basal diet and given 100 ppm cadmium via their feed for 6 wk exhibited a 69% reduction in the activity of the selenoenzyme, glutathione peroxidase, in the eye. Cadmium treatment also resulted in reductions of up to 50% in ocular calcium, irrespective of dietary selenium supplementation. Iron levels were increased by 30% in rats fed the low-selenium diet and decreased by as much as 40% in rats fed the selenium-supplemented diets, compared to animals fed identical levels of selenium without cadmium. Ocular copper levels were significantly increased only in rats fed the low-selenium diet and treated with cadmium. Ocular zinc levels were not significantly affected by dietary cadmium or selenium.

In the following two studies, a connection is shown between cadmium toxicity and anosmia (loss of smell.) Brain accumulation of injected cadmium was determined by using radioactive cadmium. Cadmium was found to accumulate in the choroid plexus, pineal gland, area postrema, trigeminal ganglia, and olfactory bulb. In the eye, cadmium accumulates in the iris, ciliary body, and choroid. It is speculated that cadmium accumulation in the olfactory bulb is related to the loss of ability to smell (anosmia) seen in workers exposed to cadmium.

Interestingly, I have a friend who developed anosmia after a fasting and cleansing diet high in green juices. He lives far from pollution in the mountains and has never smoked tobacco. This may well be good evidence that cadmium toxicity can result from excessive intake of green leafy vegetables as well as from inhaling the smoke of another green leafy vegetable, tobacco. As a possible testament to the long half-life of cadmium, his anosmia lasted for two years.

Title
Autoradiographic localization of **cadmium** in the rat brain.

Author
Arvidson B

Source
Neurotoxicology, 7(3):89-96 1986 Fall

Abstract
Adult rats were injected intravenously with $^{109}\text{CdCl}_2$ and the distribution of the isotope within the brain and neighboring nervous structures was subsequently studied by autoradiography. **Cadmium** accumulated in regions outside the blood-brain barrier such as the choroid plexus, pineal gland and area postrema, but did not appear in the brain parenchyma. Uptake of **cadmium** was observed in the trigeminal ganglia close to the nerve cells and in the olfactory bulbs. In addition, **cadmium** accumulated in the iris, ciliary body and choroid of the eye, but not in the optic nerves. The deposition of **cadmium** in the olfactory bulbs may be related to the anosmia reported in workers exposed to this metal. The possible harmful effects of accumulation of **cadmium** in restricted regions of the brain and adjacent nervous structures are discussed.

Int J Occup Med Environ Health 1998;11(3):235-45

Olfactory disorders induced by cadmium exposure: a clinical study.

Rydzewski B, Sulkowski W, Miarzynska M
ENT Department, F. Raszeja Municipal Hospital, Poznan, Poland.

Cadmium, as a highly toxic metal, found widely in industry and in the environment, is frequently included in the list of chemicals known to cause olfactory impairment. The purpose of this study was to evaluate olfaction in workers occupationally exposed to cadmium. The correlation between olfaction and concentrations of cadmium in urine, blood and in the workplace air as well as employment duration was examined in workers of the "CENTRA" S.A., an electrochemical plant in Poznan. In this plant cadmium-nickel batteries are produced, and there is chronic occupational exposure to cadmium in quantities exceeding maximum allowable concentration (MAC). Of the 73 workers who completed the evaluation, 53 people (72.7%) were smokers (10-40 cigarettes per day). The examinations revealed numerous cases of hyposmia (26.0%) and parosmia (17.8%) and one case of anosmia (1.4%). In the majority of people with olfactory disorders, hypertrophic changes in the nasal mucosa, dependent on the duration of employment, were identified. **Statistically significant relationship between olfactory impairment and cadmium concentration in blood, urine and the workplace air was observed.**

In the following study it is stated that, "Chronic inhalation of cadmium at the workplace or in cigarette smoke is associated with emphysema, a disease characterized by extensive disruption of lung connective tissue." The study shows that cadmium disrupts the production of collagen in the lungs by inhibiting fibroblast procollagen and proteoglycan production. Since collagen production is dependent upon copper and cadmium appears to be a direct antagonist of copper, copper depletion may be one of the mechanisms by which cadmium disrupts collagen production.

Am J Respir Cell Mol Biol 1998 Sep;19(3):498-506

Title: Cadmium inhibits proteoglycan and procollagen production by cultured human lung fibroblasts.

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Chronic inhalation of cadmium at the workplace or in cigarette smoke is associated with emphysema, a disease characterized by extensive disruption of lung connective tissue. **We have previously shown that cadmium, at noncytotoxic doses, inhibits fibroblast procollagen production** in vitro, with maximal inhibitory effects of 69 +/- 6% ($P < 0.01$) at 30 μM cadmium chloride (CdCl_2). **In this paper we show that at similar doses, cadmium also inhibits proteoglycan synthesis**, with values reduced by between 36 +/- 4% ($P < 0.01$) and 42 +/- 6% ($P < 0.01$) for proteoglycans secreted into the culture media and associated with the cell layer, respectively. The greatest inhibition was obtained for the major matrix-associated proteoglycans, versican, decorin, and the large heparan sulfate proteoglycans, with synthesis values reduced by between 60 and 70%. Biglycan and other heparan sulfate proteoglycans were also affected, with synthesis values reduced by between 25 and 45%. In contrast, total protein synthesis was unaffected. Furthermore, effects of cadmium at the protein level were mirrored by reduction in messenger RNA levels for $\alpha 1(\text{I})$ procollagen, versican, and decorin. **These data support the hypothesis that cadmium may play an important role in the pathogenesis of emphysema associated with chronic inhalation of cadmium fumes by inhibiting the production of connective tissue proteins.**

PMID: 9730878, UI: 98400991

The following study is very significant because it explores the mechanisms of cadmium damage to lung cells and this may give us clues about how cadmium damages the thyroid. It is shown that the cadmium induced cell injury and lipid peroxidation are inhibited by catalase and superoxide dismutase (copper, zinc based),

two antioxidant enzymes.

Furthermore it was determined that hydrogen peroxide is the main reactive oxygen species (ROS) involved. Hydrogen peroxide is the ROS which stimulates thyroid hormone production in the thyroid, so this gives us a direct connection from cadmium toxicity to increased thyroid hormone production as we see in Graves' Disease.

Also it is shown that cadmium causes mitochondrial damage by "significant dose-dependent changes of mitochondrial membrane potential." This is very significant because we have been looking for a mechanism by which the mitochondrial membrane's lithium-sodium counter transport system is disrupted. This is the mechanism which appears to transport copper into the mitochondria and may be the breakdown point where mitochondrial copper deficiency is created, thereby inducing diseases such as hyperthyroidism and manic depression. Remember that these are some long hypothetical leaps, but this could provide a testable theory of the core mechanisms involved in both hyperthyroidism and hypothyroidism. Cadmium may be the most significant toxic substance in the etiology of thyroid disease.

Cadmium-induced oxidative cellular damage in human fetal lung fibroblasts (MRC-5 cells).

Yang CF, Shen HM, Shen Y, Zhuang ZX, Ong CN

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Epidemiological evidence suggests that cadmium (Cd) exposure causes pulmonary damage such as emphysema and lung cancer. However, relatively little is known about the mechanisms involved in Cd pulmonary toxicity. In the present study, the effects of Cd exposure on human fetal lung fibroblasts (MRC-5 cells) were evaluated by determination of lipid peroxidation, intra-cellular production of reactive oxygen species (ROS), and changes of mitochondrial membrane potential. **A time- and dose-dependent increase of both lactate dehydrogenase leakage and malondialdehyde formation was observed in Cd-treated cells.** A close correlation between these two events suggests that lipid peroxidation may be one of the main pathways causing its cytotoxicity. **It was also noted that Cd-induced cell injury and lipid peroxidation were inhibited by catalase and superoxide dismutase, two antioxidant enzymes.** By using the fluorescent probe 2',7'-dichlorofluorescein diacetate, a significant increase of ROS production in Cd-treated MRC-5 cells was detected. **The inhibition of dichlorofluorescein fluorescence by catalase, not superoxide dismutase, suggests that hydrogen peroxide is the main ROS involved.** Moreover, the **significant dose-dependent changes of mitochondrial membrane potential in Cd-treated MRC-5 cells**, demonstrated by increased fluorescence of rhodamine 123 examined using a laser-scanning confocal microscope, also **indicate the involvement of mitochondrial damage in Cd cytotoxicity.** These findings provide in vitro evidence that Cd causes oxidative cellular damage in human fetal lung fibroblasts, which may be closely associated with the pulmonary toxicity of Cd.

PMID: 9294717, UI: 97440499

The following review states that

J Environ Pathol Toxicol Oncol 2001;20(2):77-88

Oxidative mechanisms in the toxicity of chromium and cadmium ions.

Stohs SJ, Bagchi D, Hassoun E, Bagchi M.

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Chromium and cadmium are widely used industrial chemicals. The toxicities associated with both metal ions are well known. However, less information is available concerning the mechanisms of toxicity. The results of in vitro and in vivo studies demonstrate that both cations induce an oxidative stress that results in oxidative deterioration of biological macromolecules. However, different mechanisms are involved in the production of oxidative stress by chromium and cadmium. Chromium undergoes redox cycling, while **cadmium depletes glutathione and protein-bound sulfhydryl groups, resulting in enhanced production of reactive oxygen species such as superoxide ion, hydroxyl radicals, and hydrogen peroxide.** These reactive oxygen species result in increased lipid peroxidation, enhanced excretion of urinary lipid metabolites, modulation of intracellular oxidized states, DNA damage, membrane damage, altered gene expression, and apoptosis. Enhanced production of nuclear factor-kappaB and activation of protein kinase C occur. Furthermore, the p53 tumor suppressor gene is involved in the cascade of events associated with the toxicities of these cations. In summary, the results clearly indicate that although different mechanisms lead to the production of reactive oxygen species by chromium and cadmium, similar subsequent mechanisms and types of oxidative tissue damage are involved in the overall toxicities.

The following study shows that cells protect themselves from cadmium toxicity by production metallothionein (MT), which is a thiol-rich protein (contains sulfur). We have seen that cadmium induces

production of hydrogen peroxide and this chemical releases free radicals which increase thyroid hormone production. Now here is evidence that sulfur groups called thiols bind with cadmium to protect cells from cadmium induced damage. Antithyroid drugs such as Tapazole and PTU contain these thiols also.

Toxicology 1995 Apr 12;98(1-3):1-13

Title: Oxidant resistance of cadmium-adapted human lung fibroblasts.

Hart BA, Prabhu RM, Eneman JD, Durieux-Lu CC, Janssen AM, Borm PJ

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Metallothionein (MT) is a metal and thiol-rich protein readily induced by cadmium (Cd) exposure. In vitro experiments have demonstrated that MT is able to serve as a scavenger of hydroxyl radicals as well as superoxide anions, albeit to a lesser extent. The role of MT as a mediator in Cd induced oxidant resistance was investigated in a nontransformed human lung fibroblast cell line (IMR-90). Cells were passaged three times either in a Cd-containing medium (8.9 microM CdCl₂) or in a medium which lacked Cd. Cellular MT content, as quantitated by a modification of the heme/109Cd binding assay, increased significantly with each passage in Cd. Immunocytochemistry studies revealed that all Cd-pretreated cells contained MT and that MT was localized in both cytoplasmic and nuclear compartments. Immunolabeling was more intense in some cells compared to others. Very slight immunolabeling was observed in physiological control cells, grown in the absence of Cd, and virtually no staining was observed in Cd-adapted or non-adapted cells when primary antibody was omitted. Using the xanthine/xanthine oxidase system as a generating system for active oxygen species, we found that the magnitude of cell injury for Cd-adapted and non-adapted fibroblasts was dependent upon oxidant concentration and duration of oxidant exposure. **Cd-adapted fibroblasts, which were characterized by over-expression of MT, were significantly more resistant to injury by active oxygen species and also exhibited a greater ability to scavenge extracellular hydrogen peroxide compared to cells with no previous history of Cd exposure.** Experiments with aminotriazole demonstrated that catalase was not a major contributor to the additional hydrogen peroxide scavenging capacity of Cd-adapted cells. The data presented in this report are consistent with involvement of MT in protecting critical cellular targets from reactive oxygen species.

PMID: 7740538, UI: 95259056

The following study shows that both zinc and selenium are key mineral antagonists to cadmium and protect cells from cadmium-induced toxicity. There is also a list of chemicals which protect cells from cadmium toxicity which includes dimethyl sulfoxide (DMSO). Ethanol was shown to not protect cells from cadmium toxicity and other studies have shown that ethanol increases cadmium accumulation into the body.

Cell Biol Toxicol 1994 Jun;10(3):191-205

Title: Antagonism of cadmium cytotoxicity by differentiation inducers.

Shopsis C

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Studies on the antagonism of toxicity can provide information about toxic mechanisms and suggest chemotherapeutic strategies. A rapid cell growth assay that measures the effects of test agents on the accumulation of cell protein (Shopsis and Eng, *Toxicol. Lett.* 1985;26:1) has been applied to studies of the antagonism of the cytotoxicity of cadmium. Exposure of Balb/c mouse 3T3 cells to 15 mumol/L Cd²⁺ for 24 h or 7 mumol/L Cd²⁺ for 48 h caused a 50% decrease in total cell protein. **Zn²⁺ and selenite ion, antagonists of Cd toxicity in vivo, antagonized Cd²⁺ cytotoxicity** when added in micromolar concentrations at the initiation of exposure to Cd²⁺. A diverse group of chemicals that can induce differentiation in vitro in cultured erythroleukemia and other cells were also found to antagonize the cytotoxic effects of Cd²⁺ to 3T3 cells. **Dimethyl sulfoxide (DMSO), hexamethylene bisacetamide, N,N-dimethyl formamide, N-methyl formamide, dimethyl acetamide, hypoxanthine, hemin, ouabain, and sodium butyrate, when added to cultures simultaneously with Cd²⁺, each antagonized Cd²⁺ toxicity.** These agents were used at concentrations equal to or lower than the concentrations at which they induce cellular differentiation. Other cytotoxicity assays and morphological studies confirmed these observations. **DMSO added as much as 6 h after the initiation of a 24-h exposure to Cd²⁺ still protected cells;** conversely, pretreatment of cultures with butyrate or DMSO for 24 h followed by their removal did not confer protection against subsequent Cd²⁺ challenge. Ethanol and methanol (noninducers of differentiation) did not antagonize Cd²⁺ cytotoxicity, and differentiation-inducing agents did not protect the cells from Zn(2+)- or Hg(2+)-induced cytotoxicity. DMSO treatment does not induce an increase in the concentrations of metallothionein or glutathione in these cells.

In the following study the authors speculate that cadmium toxicity is the result of cadmium's affinity for sulfhydryls and the cell protects itself from cadmium toxicity by increasing production of metallothionein, glutathione peroxidase (selenium compound), and sulfhydryls.

Toxicol Appl Pharmacol 1994 May;126(1):114-23

Title: Alterations in cytoskeletal organization and homeostasis of cellular thiols in cadmium-resistant cells.

Li W, Kagan HM, Chou IN

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To understand further the mechanisms of cadmium toxicity, cytoskeletal organization and homeostasis of cellular thiols were examined in cadmium-resistant cells isolated from Swiss mouse 3T3 cells by incubation in graded concentrations of CdCl₂ (Cd²⁺) in the culture medium. Cd(2+)-resistant cells displayed profound alterations in their cytoskeletal organization characterized by the appearance of many elongated, tadpole-shaped cells with a high density of microtubules (MT) and microfilaments (MF), with the former being mainly distributed along the long axis of the cell. Exposure of Cd(2+)-resistant cells to 50 microM Cd²⁺ for 16 hr did not cause apparent cytoskeletal perturbations, whereas treatment of parental cells with 5 microM Cd²⁺ for the same duration produced a severe loss of MT and smeared patches of MF. Thus, the cytoskeleton of Cd(2+)-resistant cells is markedly more preserved and protected against Cd²⁺ damage than that of their parental counterparts. **Cd(2+)-resistant cells contained a higher basal level of protein sulfhydryls (PSH) in both the cytoskeletal and cytosolic fractions than the parental cells.** Exposure to 50 microM Cd²⁺ further increased cellular PSH contents, reaching 192 and 215% of the basal levels for the cytoskeletal and cytosolic fractions, respectively. Although 5 microM Cd²⁺ exposure also elevated the amounts of PSH in parental cells, the "absolute" values were still below the corresponding basal levels in Cd(2+)-resistant cells. **Furthermore, Cd(2+)-resistant cells also exhibited enhanced basal levels of metallothionein and cellular glutathione (GSH),** amounting to 19- and 2.1-fold of the parental basal levels, respectively. **Thus, the Cd(2+)-resistant cells produced larger quantities of both protein and nonprotein thiol-containing elements than the parental cells.** Interestingly, exposure of Cd(2+)-resistant cells to 50 microM Cd²⁺ also further increased metallothionein and cellular GSH to 178 and 138% of the basal levels, respectively. **Based on the affinity of Cd²⁺ for sulfhydryls as a mechanism of Cd²⁺ toxicity, we propose that the coordinately increased levels of metallothionein, GSH, and PSH in Cd(2+)-resistant cells would provide a mechanistic basis for the homeostasis of cellular thiols which may collectively contribute to the cytoskeletal preservation by protecting the cytoskeleton from Cd²⁺ insult.**

The following study shows that transforming growth factor beta (TGF beta 1) induces a tolerance to cadmium in cultured endothelial cells.

Toxicology 1994 Mar 11;88(1-3):69-79

Transforming growth factor beta-induced tolerance to cadmium cytotoxicity in cultured vascular endothelial cells.

Kaji T, Ohkawara S, Yamamoto C, Sakamoto M, Kozuka H

Department of Environmental Science, Faculty of Pharmaceutical Sciences, Hokuriku University, Kanazawa, Japan.

We investigated whether or not **transforming growth factor beta (TGF beta 1)** affects the sensitivity to cadmium of bovine aortic endothelial cell in a culture system. Cadmium cytotoxicity was evaluated by [³H]adenine release assay. It was found that pretreatment with recombinant human TGF beta 1 (rhTGF beta 1) of the confluent cultures resulted in a reduction of cadmium cytotoxicity, suggesting that the cytokine induced a tolerance to cadmium in the cells. Such a tolerance was induced slightly by either recombinant human tumor necrosis factor alpha or recombinant human basic fibroblast growth factor but not by recombinant human interleukin-1 beta and -6; rhTGF beta 1 was the most potent inducer. rhTGF beta 1 failed to induce the tolerance in the presence of anti-rhTGF beta 1 antibody. Pretreatment with the antibody alone caused a significantly sensitive response to cadmium, suggesting that endogenous TGF beta 1 can physiologically contribute to protection against cadmium cytotoxicity in endothelial cells. The accumulation of cadmium was increased in the extracellular fraction but significantly decreased in the intracellular fraction of the cells by pretreatment with rhTGF beta 1. The cadmium content was significantly decreased in the particulate fraction but not in the cytosol fraction. Gel filtration chromatography of the cytosol fraction revealed that cadmium was bound to high-molecular-weight protein and metallothionein; both peaks were slightly increased by pretreatment with rhTGF beta 1. **It was concluded that rhTGF beta 1 induces a tolerance to cadmium in cultured endothelial cells, caused by a decrease in the cadmium accumulation in the particulate fraction of the cells. TGF beta 1 may serve as a protective factor against cadmium cytotoxicity in vascular endothelial cells.**

The following study shows that older cells are more sensitive to the toxic effects of cadmium because of reduced ability to produce metallothionein.

Exp Gerontol 1993 Jan-Feb;28(1):17-38

Metallothionein expression and stress responses in aging human diploid fibroblasts.

Luce MC, Schyberg JP, Bunn CL

Metallothioneins (MTs) are low molecular weight proteins with a high cysteine content that are inducible by heavy metals and by other conditions of environmental stress. This laboratory was investigated in human diploid fibroblasts the induction of MTs by cadmium and by dexamethasone, and the induction of heat shock proteins, as models for age-related changes in gene expression that reflect the ability of old cells to respond to environmental stress. **Old cells were more sensitive to the toxic effects of CdCl₂ in the concentration range 100-175 microM.** Analysis of ³⁵S-cysteine-labelled cell extracts by polyacrylamide gel electrophoresis and fluorography showed that in the absence of any inducer, old cells have a 3.7-fold increase over young cells in the basal level of MT. The rate and extent of induction of MT by CdCl₂ was reduced in old cells: **Exposure of old cells to 100 microM CdCl₂ for 18 h resulted in MT levels about 33% of the amount in young cells.** Northern blot analysis showed that the changes in MT protein levels occurred in parallel with changes in mRNA levels, which implicates transcriptional control as the origin of these aging changes. These young/old differences in MT synthesis were maintained in density-arrested cultures, indicating that the aging changes were not due to differences in the cell cycle status of these cell populations. The rate and extent of induction of a 68-kDa heat shock protein were also reduced in old cells, which showed an increase in basal, uninduced level of this protein similar to MT. In contrast, old cells retained the ability to synthesize MTs in response to dexamethasone at a rate similar to that in young cells.

The following study elaborates how cells develop cadmium resistance.

Life Sci 1999;65(14):PL177-82

Reduced uptake and enhanced release of cadmium in cadmium-resistant metallothionein null fibroblasts.

Yanagiya T, Imura N, Kondo Y, Himeno S

Department of Public Health and Molecular Toxicology, School of Pharmaceutical Sciences, Kitasato University, Tokyo, Japan.

Metallothionein (MT) is known to play a predominant role in the protection of cells from cadmium (Cd) toxicity. To investigate other factors involved in Cd resistance, we established Cd-resistant cell lines from simian virus 40-transformed MT null fibroblasts. Cd-resistant MT null cells, Cd-rA7 and Cd-rB5, developed approximately 10-fold resistance to Cd compared to parental cells, but showed no cross-resistance to Zn, Cu, Hg, Ni, As, cisplatin or H₂O₂. Accumulation of Cd in the resistant cells was 13-18% of that of parental cells after treatment with Cd for 24 h. A short-term experiment revealed that the rate of Cd incorporation into the Cd-resistant cells was suppressed, and the rate of Cd release was enhanced in the resistant cells compared with that of parental cells. **These results indicate that the altered transport of Cd, slow uptake and rapid release, may confer resistance to Cd on the Cd-resistant cells established from MT null fibroblasts.**

PMID: 10530804, UI: 99458387

The following study should be a concern to anyone reading this on a computer. Three novel compounds which are used in the manufacture of computers were tested for toxicity. These compounds may be inhaled by workers in the semiconductor industry or users of computers. While I believe that users of computers would have very little exposure, it would be good to find out how much.

The most toxic of the three tested was found to be cadmium telluride and presumably the toxicity is due to the cadmium. I consider it another example of how cadmium from industrial uses can get into our bodies and probably cause thyroid disruption.

Comparative pulmonary absorption, distribution, and toxicity of copper gallium diselenide, copper indium diselenide, and cadmium telluride in Sprague-Dawley rats.

Morgan DL, Shines CJ, Jeter SP, Blazka ME, Elwell MR, Wilson RE, Ward SM, Price HC, Moskowitz PD

National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina 27709, USA.

Copper gallium diselenide (CGS), copper indium diselenide (CIS), and cadmium telluride (CdTe) are novel compounds used in the photovoltaic and semiconductor industries. This study was conducted to characterize the relative toxicities of these compounds and to evaluate the pulmonary absorption and distribution after intratracheal instillation. Female Sprague-Dawley rats were administered a single equimolar dose (70 mM) of CGS (21 mg/kg), CIS (24 mg/kg), CdTe (17 mg/kg), or saline by intratracheal instillation. Bronchoalveolar lavage fluid (BALF) protein, fibronectin, inflammatory cells, lung hydroxyproline, and tissue distribution were measured 1, 3, 7, 14, and 28 days after instillation. Relative lung weights were significantly increased in CIS- and CdTe-treated rats at most time points. **Inflammatory lesions in the lungs consisting of an influx of macrophages, lymphocytes, and PMNs were most severe in CdTe-treated rats**, intermediate in CIS-treated rats, and minimal in rats receiving CGS. **Hyperplasia of alveolar type 2 cells was present in CIS- and CdTe-treated rats and was greatest in CdTe-treated rats. Pulmonary interstitial fibrosis was observed in CdTe-treated rats at all time points.** All three

compounds caused marked increases in total BALF cell numbers, with the greatest increase observed in CIS-treated rats. BALF protein, fibronectin, and lung hydroxyproline were significantly increased in all treated animals and were highest in CdTe-treated animals. There was no apparent pulmonary absorption or tissue distribution of CGS. Indium levels increased in extrapulmonary tissues of CIS-treated rats, although Cu and Se levels remained unchanged. **CdTe was absorbed from the lung to a greater extent than CGS and CIS. Cd and Te levels decreased in the lung and increased in extrapulmonary tissues. Of these compounds CdTe presents the greatest potential health risk because it causes severe pulmonary inflammation and fibrosis and because it is readily absorbed from the lung may potentially cause extrapulmonary toxicity.**

The following study helps give us an idea about how toxic cadmium is in relation to other metals with known or presumed biological function. Cadmium is three times more toxic than arsenic. However, if it could be shown that cadmium is an essential nutrient, as I suspect all of the other metals mentioned are, then it also can give us an idea about how much we might need of it in relation to the other minerals.

J Toxicol Environ Health 1990 May;30(1):23-31

Teratogenicity of metals to chick embryos.

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The present study examines the effects of heavy metals on chick embryogenesis. **The metals included were cadmium, arsenic, cobalt, copper, indium, iron, manganese, and molybdenum.** Salts of each of the metals were dissolved in saline and injected into the air sacs on d 2 of incubation. Dose levels varied with the metal to be tested. Control eggs were injected with an equivalent volume of saline (0.1 ml/egg). On d 14, the live embryos were removed from the eggs and examined for gross malformations. **From the LD50 values, the toxicity relationship between the metals is cadmium greater than arsenic greater than cobalt greater than copper greater than indium greater than molybdenum greater than manganese greater than iron. The LD50 values were 3, 9, 38, 58, 121, 333, 765, and 1185 micrograms/egg, respectively.** The gross malformations observed were reduced body size, micromelia, twisted neck, hemorrhage, everted viscera, and microphthalmia. Arsenic and cobalt were observed to be more teratogenic than other metals. This study showed that the metals tested were both toxic and teratogenic to varying degrees in chick embryogenesis.

The following study shows that as cadmium blood levels increase, TSH increases and FT4 decreases. Another study with implications that cadmium causes thyroid disease.

Environ Health Perspect 1999 Oct;107(10):843-9

Exposure to polychlorinated biphenyls and levels of thyroid hormones in children.

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As part of an epidemiologic study on exposure to a toxic waste incineration plant we investigated whether blood concentrations of polychlorinated biphenyls (PCBs), lead, and cadmium, as well as concentration of mercury in 24-hr urine samples were associated with thyroid hormone status. As an indication of status, we determined levels of thyroid-stimulating hormone (TSH), free thyroxine (FT(4)), and free triiodothyronine (FT(3)) in children living in households where [less than/equal to] 10 cigarettes were smoked per day. Eight PCB congeners (PCBs 101, 118, 138, 153, 170, 180, 183, and 187) were measured in whole blood samples. Of these, seven congeners (PCB 101 was not detected in any sample) and the sum of all PCB congeners were analyzed as predictors for thyroid hormone status in separate linear regression models adjusted for potential confounders. In addition, the possible effects of cadmium, lead, and mercury on levels of thyroid hormones were examined. Blood concentrations and information on questionnaire data were available for 320 children 7-10 years of age. We found a statistically significant positive association between the mono-ortho congener PCB 118 and TSH as well as statistically significant negative relationships of PCBs 138, 153, 180, 183, and 187 to FT(3). There was no association for the PCB congeners and FT(4). **Blood cadmium concentration was associated with increasing TSH and diminishing FT(4).** Blood lead and urine concentration of mercury were of no importance to thyroid hormone levels. The results stress the need for future studies on the possible influences of PCB and cadmium exposure on thyroid hormones, particularly in children. These studies should also take neurologic development into account.

CADMIUM CHELATORS

The following study indicates that DMPA, but not DMSA or DMPS, may be an effective chelator for cadmium removal from the body.

Fundam Appl Toxicol 1990 Apr;14(3):598-607

Determination and metabolism of dithiol chelating agents. VII. Biliary excretion of dithiols and their interactions with cadmium and metallothionein.

Zheng W, Maiorino RM, Brendel K, Aposhian HV

Department of Pharmacology and Toxicology, University of Arizona, Tucson 85721.

N-(2,3-Dimercaptopropyl) phthalamidic acid (DMPA), meso-dimercaptosuccinic acid (DMSA), and 2,3-dimercapto-1-propanesulfonic acid (DMPS) are dithiol chelating agents with antidotal activity for lead, mercury, arsenic, and other heavy metals. The biliary excretion of these compounds was studied in male Sprague-Dawley rats. After iv administration of DMPA, 72% of the injected dose was recovered in the bile. Half of the recovered DMPA was in the unaltered form (parent compound) and the other half was in the altered form (parent compound recovered after chemical reduction by DTT). An altered, presumably disulfide, form of DMPS was found in the bile. Neither unaltered nor altered DMSA was detected in the bile. DMPA (0.10 mmol/kg), given to rats 3 days after exposure to Cd, elicited within 30 min a 20-fold increase in biliary Cd excretion. **The increase of biliary Cd by DMPA was dose-related and not due to an increase of bile flow rate. DMSA and DMPS did not significantly affect the biliary excretion of Cd.** Incubation of DMPA or DMSA with Cd-saturated metallothionein (MT) resulted in the removal of Cd from MT. DMPA was more active than DMSA in this respect. **The evidence strongly supports the mechanism that the increase of biliary cadmium following DMPA administration is the result of DMPA entering cells and mobilizing and removing the cadmium from MT. The removal of cadmium from metallothionein by dithiol chelating agents provides another dimension to their mechanisms of action and may provide an important new tool for the study of cadmium as well as metallothionein.**

The following study indicates that BAL is an effective chelator of cadmium.

J Toxicol Environ Health 1980 Mar;6(2):393-401

Biliary excretion of cadmium in rat. VI. Mobilization of cadmium from metallothionein by 2,3-dimercaptopropanol.

Cherian MG

Cadmium was preferentially bound to metallothionein in tissues 24 h after CdCl₂ injection. **Of a number of chelating agents examined, only 2,3-dimercapto-1-propanol (BAL) was effective in mobilizing Cd from metallothionein into bile.** Structurally similar dithiols such as 1,3-dimercaptopropanol and 2,3-dimercapto-1-propanesulfonic acid were not effective. Diethylenetriamine pentaacetic acid increased only the urinary excretion of Cd. **Biliary excretion of Cd increased with increasing dose of BAL, and there was a concurrent decrease in hepatic Cd levels without any increase in renal concentration.** BAL was effective even 14 d after Cd injection. The form of Cd excreted in the bile after BAL injection in chronic exposure has not yet been characterized. Initial studies suggested that it was not metallothionein but was a low-molecular-weight Cd complex, probably with BAL.

The following study demonstrates the effectiveness of using alpha lipoic acid (a supplement available in a health food store and which I have used) in protecting the liver from cadmium toxicity.

Jpn J Med Sci Biol 1996 Apr;49(2):39-48

Relationship between glutathione and DL alpha-lipoic acid against cadmium-induced hepatotoxicity.

Sumathi R, Baskaran G, Varalakshmi P

Department of Medical Biochemistry, Dr. ALM Post Graduate Institute of Basic Medical Sciences, University of Madras, India.

Cadmium, a divalent metal toxicant, preferentially localizes in hepatocytes and causes liver injury. **DL alpha-lipoic acid is a dithiol which is effective in rendering protection against cadmium-associated liver damage, by virtue of its two sulfhydryl moieties.** Lipoate was administered to cadmium-exposed rats which were either prior administered with buthionine sulfoximine to deplete liver glutathione or not. During lipoate treatment, significant protection was rendered against cadmium toxicity even under glutathione-depleted experimental condition. **This highlights the antioxidant property of lipoic acid and its efficacy in mitigating cadmium-associated liver assault even in the absence of glutathione synthesis.**

FOOD SOURCES OF CADMIUM

The following study is important because it states that cadmium absorption is increased by co-administration of milk and in conjunction with iron deficiency. The author also states that mercury accumulation is increased by a factor of ten in suckling pigs and that milk increases the bioavailability of mercury. If the

absorption of cadmium and mercury are increased significantly by milk, this is interesting because of the fact that the factor in milk that might cause this is estrogen.

We have seen that females accumulate cadmium and mercury at a much higher rate than males and it seems that estrogen is an accelerator of heavy metal (and maybe all metal) accumulation. Milk may also increase heavy metal accumulation by providing additional estrogen. It could be other factors in milk, but this hypothesis needs to be investigated.

The author states that cadmium toxicity can cause microcytic hypochromic anemia, a type of anemia where the red blood cells are both smaller and have less hemoglobin. We have seen that anemia is highly associated with thyroid disease.

Z Ernährungswiss 1990 Mar;29(1):54-73

Title: The toxicological estimation of the heavy metal content (Cd, Hg, Pb) in food for infants and small children

[Article in German]

Schumann K

Walther-Straub-Institut für Pharmakologie und Toxikologie der Ludwig-Maximilians-Universität, München, FRG.

There are differences between young and adult organisms regarding toxicokinetic aspects and clinical manifestations of heavy metal intoxications. **Chronically, toxic Cd intake causes a microcytic hypochromic anemia in young rats at lower exposure levels and after shorter exposure periods than in adult animals. Cd absorption is increased by co-administration of milk and in conjunction with iron deficiency.** After long exposure periods toxic Cd concentrations accumulate in the kidney cortex; this process starts very early in life. In 3-year-old children Cd concentrations in the kidney can reach up to one-third of those found in adults. Hg⁺⁺ and methyl-Hg can cause Hg encephalopathy, and frequently cause mental retardation in adults. **Correspondingly, Hg⁺⁺ accumulation in the brains of suckling rats is approx. 10 times higher than in grown animals. Milk increases the bioavailability of Hg⁺⁺.** In suckling rats Hg is bound to a greater extent to ligands in the erythrocytes. Methyl-Hg concentrations in breast milk reach 5% of those in maternal plasma and that is a severe hazard for breastfed children of exposed mothers. Toxic Pb concentrations can lead to Pb encephalopathy. A high percentage of surviving children have seizures and show signs of mental retardation. Anemia and reduced intelligence scores were recently observed in children after exposure to very low levels of Pb. Pb absorption is increased in children and after co-administration of milk. There are no definite proofs for carcinogenesis or mutagenesis after oral exposure to Cd, Hg, and Pb in man. Heavy metal concentrations were found in the same order of magnitude in commercial infant formulas and in breast milk. When infant formulas are reconstituted with contaminated tap water, however, Pb and Cd concentrations can be much higher. The average heavy metal uptake from such diets exceeds the provisional tolerable weekly intake levels set by the WHO for adults, calculated on the basis of an average food intake and a downscaled body weight. These considerations do not even provide for differences in absorption and distribution or for the increased sensitivity of children to heavy metal exposure. However, dilution effects for essential heavy metals were observed in fast-growing young children; this effect might be extrapolated to toxic metals. These theoretical considerations are compared with epidemiological evidence. A health statistic from Baltimore shows a decline of Pb intoxications in infants. This observation correlates with a simultaneous decline in exposure to Pb which was due, for example, to decreased use of lead dyes in house paints and the abolition of tin cans for infant food.

The following study indicates that wheat bran is preferable to sugar-beet fiber and carrots to limit gastrointestinal absorption of cadmium.

Br J Nutr 1998 Aug;80(2):205-11

Accumulation of cadmium from wheat bran, sugar-beet fibre, carrots and cadmium chloride in the liver and kidneys of mice.

Lind Y, Engman J, Jorhem L, Glynn AW

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The gastrointestinal absorption and organ distribution of Cd after exposure for 9 weeks to three fibre-rich foodstuffs (wheat bran, sugar-beet fibre and carrots) were determined in mice. Groups of eight mice were given a diet containing 0.05 mg Cd/kg from wheat bran, sugar-beet fibre, carrots or CdCl₂ mixed in a semi-synthetic, low-Cd (< 0.007 mg/kg) feed. A control group was fed on the low-Cd semi-synthetic feed. The water consumption, food consumption and the weight of the animals were monitored throughout the study. The feed was changed once weekly and Cd was analysed in the feed at each change. myo-Inositol phosphates (hexa-, penta-, tetra- and tri-) and Zn, Cu, Fe and Ca were also analysed in the diets. After 9 weeks, the mice were killed and liver and kidneys were sampled and analysed for Cd. **The group receiving the wheat-bran diet had significantly lower fractional Cd accumulation (% total Cd intake) in the liver and kidneys than the other groups, indicating a lower fractional absorption of Cd.** The wheat-bran diet had markedly higher levels of inositol hexa- and pentaphosphates (phytates) and a Zn level that was twice as high as those in the other diets. The higher levels of myo-inositol hexa- and pentaphosphates in the wheat-bran diet most probably contributed more to the lower fractional absorption of Cd than the elevated Zn level, due to the formation of insoluble Cd-phytate complexes. **Compared with the wheat-bran diet, the sugar-beet-fibre and carrot diets contained very low levels of myo-inositol penta- and hexaphosphates, and consequently the fractional Cd absorption from these diets was higher.**

The above study suggested to me that cadmium may accumulate in the liver and kidneys of animals and it might be wise to avoid eating these organs to minimize your cadmium intake. The following study supports this idea. In a pristine area of Canada, eating liver and kidneys from moose kidney and liver can greatly increase dietary cadmium intake. Also note that in this relatively environmentally pure area, the cadmium intake was estimated to be about 136 micrograms per week. Of this amount only about 16 micrograms is from smoking tobacco (but this may be an average of smokers and non-smokers). Selenium is used to eliminate cadmium, so removing 136 mcg of cadmium a week will use up at least 193 mcg of selenium a week, or about 28 mcg per day. Considering that other toxic metals like mercury also use up selenium for detoxification, the drain on selenium can be very significant. In a more polluted area where selenium is low in the food supply, selenium deficiency could easily result. Conclusion: avoid eating kidney and liver to keep cadmium intake low.

Risk assessment of cadmium exposure in Fort Resolution, Northwest Territories, Canada.

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Centre for Indigenous Peoples' Nutrition and the Environment (CINE), McGill University, Ste-Anne-de-Bellevue, Quebec, Canada.

The aim of this study is to investigate the cadmium (Cd) exposure level from traditional food in Fort Resolution, Northwest Territories. We used 24-h dietary recalls and traditional food use frequency to obtain information on traditional food consumption, and analysed cadmium concentrations in traditional food. We also estimated total cadmium intake via market and traditional food, and cigarette smoking. Traditional food accounted for only 10% of the dietary energy. About 30 species of wildlife and plants were used. The most important foods in the community were moose, caribou, and whitefish. The range of cadmium concentrations measured was 0 to 1869 micrograms/g wet weight, with the lowest found in cranberry, and the highest in moose kidney. Cadmium concentrations in traditional food groups were comparable with those of Canadian market food. Highest levels of cadmium were found in the liver and kidney of caribou and moose. Cadmium intakes from traditional food estimated by dietary recall ranged from 0.01 to 1713 micrograms/g/day/person. Average cadmium intakes for women and men from traditional food were estimated to be 9% and 6% respectively, of the Provisional Tolerable Weekly Intake (PTWI, 400-500 micrograms) established by the World Health Organization. The average cadmium inhaled from cigarette smoking was 2.31 +/- 1.00 micrograms/day/person. There was no difference between the total cadmium intakes of smokers and nonsmokers. The total cadmium intake via market and traditional food and cigarette smoking was 136.6 micrograms/ week, which was lower than the PTWI. However, about 20% of the population may consume caribou and moose organ more frequently than the others. The potential health effects on this sub-population needs further clarification.

The following study suggests that the maximum dietary intake of cadmium should be 30 mcg per day (210 mcg per week). When you compare the average intake in the prior study, the average person living in northern Canada is dangerously close to the point where toxicity will occur. This means that many people in that area and in more industrial areas are consuming toxic amounts of cadmium.

Br J Nutr 2000 Dec;84(6):791-802

Safe levels of cadmium intake to prevent renal toxicity in human subjects.

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The present review attempts to provide an update of the scientific knowledge on the renal toxicity which occurs in human subjects as a result of chronic ingestion of low-level dietary Cd. It highlights important features of Cd toxicology and sources of uncertainty in the assessment of health risk due to dietary Cd. It also discusses potential mechanisms for increased susceptibility to Cd toxicity in individuals with diabetes. Exposure assessment on the basis of Cd levels in foodstuffs reveals that vegetables and cereals are the main sources of dietary Cd, although Cd is also found in meat, albeit to a lesser extent. Cd accumulates particularly in the kidney and liver, and hence offal contains relatively high amounts. Fish contains only small quantities of Cd, while crustaceans and molluscs may accumulate larger amounts from the aquatic environment. Data on Cd accumulation in human kidney and liver obtained from autopsy studies are presented, along with results of epidemiological studies showing the relationship between renal tubular dysfunction and kidney Cd burden. These findings suggest that a kidney Cd level of 50 microg/g wet weight is a maximum tolerable level in order to avoid abnormal kidney function. This renal Cd burden corresponds to a urinary Cd excretion of 2 microg/d. Accordingly, safe daily levels of Cd intake should be kept below 30 microg per person. Individual variations in Cd absorption and sensitivity to toxicity predicts that a dietary Cd intake of 30 microg/d may result in a slight renal dysfunction in about 1% of the adult population. The previous guideline for a maximum recommended Cd intake of 1 microg/kg body weight per d is thus shown to be too high to ensure that renal dysfunction does not occur as a result of dietary Cd intake.

The following study corroborates data that indicates that green leafy vegetables have a higher cadmium content than most foods such as grains. Interestingly, soy beans were found to be much higher in cadmium than other beans. Another reason not to eat soy.

Sci Total Environ 1998 Sep 18;220(2-3):137-45

Lead and cadmium contents in cereals and pulses in north-eastern China.

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Department of Public Health, Kyoto University, Faculty of Medicine, Kyoto, Japan.

It is known that, unlike Japanese, Koreans or southern Chinese who depend on rice as a major source of energy for daily life, people in north-eastern China rely not only on rice, but on wheat and other cereals and to a lesser extent also on pulses. Cereal and pulse samples were collected from open markets in north-eastern China, and analyzed by inductively-coupled plasma spectrometry (ICP-MS) for two potentially hazardous heavy metals--lead (Pb) and cadmium (Cd). The average Pb level in cereals (31.3 ng Pb/g as a geometric mean) and that of pulses (25.7 ng Pb/g) were similar to each other with no significant difference. Among the cereals, Pb contents were higher in foxtail millet (54.3 ng/g) and lower in maize (35.4 ng Pb/g; grain and flour in combination), wheat flour (28.8 ng Pb/g) and rice flour (22.7 ng Pb/g). Lead levels in two important types of pulses, kidney bean and soybean (24.6 and 30.8 ng Pb/g, respectively), were comparable to the levels in rice and wheat. **In contrast, Cd levels were substantially higher in pulses (55.7 ng Cd/g) than in cereals (9.2 ng Cd/g), and among the pulses, Cd in soybean (55.7 ng Cd/g) was significantly higher than that in kidney bean (23.8 ng Cd/g).** The possible public health implication of the Pb and Cd levels, especially the high Pb level in foxtail millet (54.3 ng Pb/g) and the high Cd level in soybean (73.5 ng Cd/g), is discussed.

Germany is an industrialized country with high rates of thyroid disease. The following study shows the relative concentrations of cadmium in various foods in Germany. As expected, some lettuce samples showed

high levels of cadmium, possibly as a result of using sewage sludge as a fertilizer. Surprisingly to me, breads, cakes, and pastries were also quite high in cadmium. I am wondering if the grain milling process or some other mechanical process introduces cadmium. While most meats are low in cadmium, liver and kidney are particularly high.

Food Addit Contam 1996 Apr;13(3):359-378

Oral cadmium exposure of adults in Germany. 1: Cadmium content of foodstuffs and beverages.

Muller M, Anke M, Hartmann E, Illing-Gunther H

Friedrich Schiller University Jena, Biological-Pharmaceutical Faculty, Institute of Nutrition and Environment, Germany.

The cadmium contents of 94 and 105 foodstuffs bought in six-fold repetition in 1988 and in nine-fold repetition in 1991, respectively were analysed within the framework of a market-basket study. These foodstuffs were typical of German eating habits. Additionally, 170 samples of drinking water were investigated. The cadmium concentrations of the foodstuffs were comparable with results of recent studies carried out in Europe and North America. Fruit, milk and dairy products, sugar and sugar-rich foodstuffs as well as beverages showed mean cadmium contents ≤ 5 ng/g fresh matter or ng/ml, respectively. The cadmium content of meat, sausage, fish and tinned fish was also low. Pork and beef, the most important kinds of meat, contained 5.4 and 2.5 ng/g on average. The majority of the vegetables investigated, including potatoes, had cadmium concentrations < 25 ng/g. **However, individuals samples of lettuce showed very high cadmium levels. The cadmium content of bread, cakes and pastries as well as farinaceous products were within the range of 20-40 ng/g. The most important bread, cakes and pastries (wheat and rye bread, toasted bread, rolls) contained 25-35 ng/g.** A median cadmium concentration of 0.2 micrograms/l was found in the drinking water. **As expected, liver and kidneys showed the highest cadmium levels of 73 and 204 ng/g, respectively on average.**

Another study on cadmium in bread.

Title: Lead and cadmium contents in Finnish breads.

Tahvonen R, Kumpulainen J

Agricultural Research Centre of Finland, Central Laboratory, Jokioinen.

A total of 647 breads from nine bakeries were pooled into 48 representative samples. After wet digestion in concentrated HNO₃, the contents of lead and cadmium were determined using electrothermal atomic absorption spectrometry with Zeeman effect background correction and (NH₄)H₂PO₄ matrix modification. The mean lead and cadmium contents found in the various types of bread were: rye bread 16 and 14, coffee bread 19 and 23, French bread 8 and 27, whole wheat bread 8 and 30, mixed bread group I 17 and 27, and mixed bread group II 14 and 28 micrograms/kg. The mean and median lead contents of all breads were 14 and 8 micrograms/kg. The samples showed a very high variation in their lead contents. In the present study, the lead content found in Finnish breads was much lower than that in the late 1970s. The mean and median cadmium contents in all of the bread samples analysed were 24 and 25 micrograms/kg. The cadmium content of rye breads was clearly lower than that of the other bread types studied. The content of cadmium in the different types of bread was at about the same level as that reported in Finnish breads in the late 1970s.

The title of the following study indicates that coffee and tea may contain significant amounts of cadmium, however there is no abstract.

Title: **Cadmium and cobalt in tea and coffee and their relationship to cardiovascular disease.**

Horwitz C, Linden SE van der

No Abstract.

PMID: 4814501, UI: 74107894

Carrots are high in cadmium (and lead) but steps can be taken to reduce the cadmium content: peeling the skin, soaking in water, and cooking all reduce the cadmium content. It may be a good idea to avoid carrots and carrot juice if you have thyroid disease.

Rocz Panstw Zakl Hig 1997;48(2):187-92

[The influence of culinary processing on content of lead and cadmium in carrots].

[Article in Polish]

Wieczorek C, Kostrzewa M

Zaklad Technologii Gastronomicznej, Wydzial Zywnienia Czlowieka oraz Gospodarstwa Domowego, Warszawa.

The research was performed to determine both safety of carrot dishes consumption taking into account lead and cadmium intake and prospect of lowering content of these elements in carrot during culinary processing. Different but unspecified varieties of investigated carrot came from the Warsaw market and from allotments and fields in Upper Silesia. Lead and cadmium level was determined in raw material as well as the elements' distribution in different parts of carrot root. The impact of initial treatment including peeling and soaking in water of the crumbled vegetable was studied. The carrot was cooked traditionally beginning with boiling or cold water. Lead and cadmium content were determined using atomic absorption spectrophotometry for extracts of APDC complexes. The investigated raw material contained little lead (an average 0.019 mg/kg) and cadmium (average 0.015 mg/kg). Both elements are distributed in layers in entire carrot root. **The highest concentration of both lead and cadmium can be found in the skin (0.075 mg Pb and 0.0115 mg Cd/kg skin), lower in parenchyma (0.028 mg Pb and 0.066 mg Cd/kg parenchyma) and the lowest in the core (0.027 mg Pb and Cd/kg core).** Because of unequal concentration of both elements in each layer, peeling eliminates up to 25% lead and about 19% cadmium. Keeping carrot in water showed a tendency to diminish the level of both elements in raw material. Soaking carrot for 24 h made it shed 40% of lead and 67% of cadmium. Cooking process decreased both metal's concentration in the vegetable. The traditional cooking method diminished lead content by 6-47% and cadmium content by 35-44%.

Chocolate is high in copper but for some reason it does not seem to be a good food for hypers which the high copper content would suggest. Because of this and other reasons, I developed a suspicion that chocolate is

high in cadmium. Searching for medical studies on cadmium and chocolate led me to only two studies. The first study below is very suggestive that my suspicion is correct and that cocoa beans may be high in both cadmium and lead. The second study confirms that chocolate is high in cadmium (and also nickel). It's possible that the cadmium is introduced to the cocoa during processing, possibly by contact with galvanized containers, and is not natural to the food.

Nahrung 1987;31(5-6):635-6

Lead and cadmium content in cocoa beans (short communication).

Prugarova A, Kovac M

Food Research Institute, Bratislava, Czechoslovakia.

The choice of cocoa beans as the experimental and sample material for study of the contamination with lead and cadmium was inspired by high Pb and Cd limits in foods made on its basis (cocoa powder, chocolate) as well as by the relatively high proportion of these foods in human nutrition. For Cd, the limits in food products are within the range of 0.01 mg X kg⁻¹ (milk) to 1.0 mg X kg⁻¹ (kidneys) whereas the limits for lead range between 0.1 mg X kg⁻¹ (e.g. milk) and 10.0 mg X kg⁻¹ (e.g. tea, yeast, crustaceans, molluscs). Limits for Pb and Cd in foods made on cocoa bean basis are given in Table 1.

Food Addit Contam 1994 May-Jun;11(3):351-63

Beverages as a source of toxic trace element intake.

Pedersen GA, Mortensen GK, Larsen EH

National Food Agency of Denmark, Central Laboratory, Soborg.

Beverages of different kinds have been investigated for their content of lead, cadmium, nickel, chromium, arsenic and mercury. About a ten times higher lead concentration was found in wine than in most other beverages. **Cocoa was high in cadmium and nickel and some vegetable juices contained high levels of nickel.** The daily intake of trace elements from beverages was estimated. Wine was still the most significant source of lead even if the bottles did not have lead capsules. By consumption of half a bottle per day the daily intake of lead would be doubled and it would contribute 12% of Provisional Tolerable Weekly Intake. Cocoa is an important source of cadmium and nickel, and consumption of tea as well as vegetable juices could increase the nickel intake significantly. The data are compared to Danish maximum limits on lead and cadmium.

MACULAR DEGENERATION AND CADMIUM

The following study states that macular degeneration is the leading cause of visual impairment in the elderly and that the adverse effect of smoking (a known inducer of cadmium toxicity) is well established.

J Med Genet 2000 Feb;37(2):83-7

Genetic susceptibility to age related macular degeneration.

Yates JR, Moore AT

Department of Medical Genetics, University of Cambridge, Box 134, Addenbrooke's Hospital, Cambridge CB2 2QQ, UK.

Age related macular degeneration (AMD) is the leading cause of visual impairment in the elderly and a major cause of blindness in the developed world. The disease can take two forms, geographic atrophy and choroidal neovascularisation. The pathogenesis of AMD is poorly understood. **There are undoubtedly environmental and other risk factors involved and the adverse effect of smoking is well established.** Several studies have shown that genetic factors are important but leave uncertainty about the magnitude and nature of the genetic component and whether it varies with the type of AMD. Several hereditary retinal dystrophies show similarities to AMD and these genes are potential candidate susceptibility genes. Particular interest has focused on the ABCR gene which is responsible for autosomal recessive Stargardt macular dystrophy. It has been claimed that heterozygotes for ABCR mutations are predisposed to AMD but the data are conflicting. Studies of the genes responsible for autosomal dominant Sorsby fundus dystrophy, Doyme honeycomb retinal dystrophy, and Best disease have given negative results. In one large AMD family, linkage has been reported to markers in 1q25-q31. Recent data suggest that the ApoE epsilon4 allele may be associated with reduced risk of AMD. A better understanding of the genetic factors in AMD would contribute to understanding the pathogenesis. If those at risk could be identified it may be possible to modify lifestyle or develop novel therapies in the presymptomatic stage to prevent disease or decrease its severity.

Following is an excellent twin case study on the effects of smoking on thyroid disease. The key conclusions are that cumulative cigarette smoking is associated with autoimmune thyroid disease, particularly Graves' Disease with ophthalmopathy, and that smoking (think cadmium) leads to autoimmune Graves' Disease when iodine intake is adequate and autoimmune Hashimoto's Thyroiditis when iodine intake is inadequate. Particularly when we factor in other sources of cadmium toxicity, this is very powerful evidence that cadmium is the prime source of autoimmune thyroid disease.

Cigarette Smoking and Risk of Clinically Overt Thyroid Disease

A Population-Based Twin Case-Control Study

Thomas Heiberg Brix, MD; Pia Skov Hansen, MD; Kirsten Ohm Kyvik, MD, PhD; Laszlo Hegedüs, MD

Background The effects of cigarette smoking on the thyroid gland have been studied for years. However, the effect of smoking on thyroid function and size is still controversial.

Objective To determine the impact of cigarette smoking on the development of clinically overt thyroid disease.

Methods Matched case-control study of 132 same-sex twin pairs (264 individuals) discordant for clinically overt thyroid disease, ascertained from a population-based nationwide twin register. Information on thyroid disease and smoking habits was gathered by questionnaire, and the patients' endocrinologist or general practitioner verified the diagnosis.

Results Overall, smoking was associated with an increased risk of developing clinically overt thyroid disease (odds ratio, 3.0; 95% confidence interval, 1.4-6.6; $P=.003$). This association remained statistically significant in monozygotic and dizygotic disease-discordant pairs. The effect of smoking was more pronounced in monozygotic vs dizygotic pairs (odds ratio, 5.0 vs 2.5; $P=.04$ for both). Essentially similar results were obtained after subdividing the twin pairs into groups discordant for clinically overt autoimmune (49 pairs) and nonautoimmune (83 pairs) thyroid disease. Among twin pairs concordant for smoking, probands with clinically overt autoimmune thyroid disease smoked significantly more than did their healthy co-twins (17 pairs; $P=.03$), whereas no difference was found between probands with nonautoimmune thyroid disease and their healthy co-twins (34 pairs; $P=.20$).

The most striking effect of smoking on the thyroid is its strong association with Graves ophthalmopathy and Graves disease without ophthalmopathy, although the latter association is weaker. Although previous studies have repeatedly shown a clear association between smoking and Graves disease, with and without ophthalmopathy, they have come to somewhat different conclusions regarding a possible correlation between smoking severity and the prevalence or severity of Graves disease. In the present study, we found that, among twin pairs concordant for smoking, probands with clinically overt Graves disease smoked significantly more than their healthy co-twins. This finding is consistent with results from other studies demonstrating a positive correlation between cumulative cigarette consumption (counted in pack-years) and the development of Graves disease in genetically susceptible individuals. Such a correlation could not be demonstrated in clinically overt nonautoimmune thyroid disease, indicating that a dose effect of smoking is a risk factor in autoimmune thyroid disease, but not in thyroid disease in general.

In fact, recent evidence indicates that the predominant effect of smoking on the thyroid is goitrogenic or antithyroid when iodine intake is low, and immunogenic when intake is adequate. In our study, all participants were residents of Denmark, an area with borderline iodine deficiency but no endemic goiter.

Conclusions Smoking is associated with an increased risk of developing clinically overt thyroid disease. Furthermore, our data suggest that cumulative cigarette consumption is a risk factor, most pronounced in autoimmune thyroid disease.

Arch Intern Med. 2000;160:661-666

Information contributed by Christine Cline:

Since John has made us aware of a cadmium connection, I decided to check into it. I found this info in the 1996 edition of the Nutrition Almanac:

"Cadmium is a toxic trace mineral that has many similarities to zinc. There is no biological function for this element in humans. Its toxic effects are kept under control in the body by the presence of zinc.

"Food refining processes disturb the important cadmium-zinc balance. In WHOLE wheat, cadmium is present in proportion to zinc in a ratio of 1 to 20.

"Cadmium is found primarily in refined foods such as flour, rice, and white sugar. It is present in the air in cigarette smoke and in air pollution such as found around zinc factories. In addition, soft water usually contains higher levels of cadmium than does hard water. Soft water, especially if it is acid, leaches cadmium from metal water pipes.

"The liver and kidneys are storage areas for both cadmium and zinc. The total body concentration of cadmium increases with age and varies in different areas of the world. It is very poorly absorbed, so in normal dietary and environmental circumstances should not be a problem.

"When a deficit of zinc occurs in the diet, the body may make it up by storing cadmium instead. If the daily intake of zinc is high, zinc will be stored and cadmium will be excreted.

-- "Cadmium also interferes with the absorption of copper."

-- "Zinc is a natural antagonist to cadmium."

-- "When zinc antagonizes cadmium, protection from cancer may occur."

-- "Cadmium can be detoxified with selenium."

-- "Alginates (found in seaweed) bind to cadmium and remove it from the body, a process which could prevent poisoning."

"Cadmium poisoning is a very subtle process and can accumulate over a lifetime. Cadmium deposits in the kidneys, causing kidney damage, and settles into arteries, raising blood pressure and resulting in atherosclerosis.

"Cigarette smoke contains substantial amounts of cadmium. One pack of cigarettes deposits 2 to 4 micrograms into the lungs of a smoker while some of the smoke passes into the air to be inhaled by smokers and nonsmokers alike."

I think John is on to something with this cadmium subject. I'm unable to find info that relates it directly to the thyroid, but that doesn't mean the info is not out there. Cadmium is directly related to copper and zinc--and copper and zinc are big players in thyroid function.

Note re smoking:

John states in his new website, under nutrients and toxics: "Maybe one of the reasons people smoke is to get cadmium into their bodies."

I've read in thyroid books that some hyperT patients START smoking AFTER they are diagnosed with Graves'. I can testify to that myself. Was diagnosed at age 29 and started smoking cigarettes for the first time when I was 31.

I still smoke (yeah I know, I know), but I had figured it didn't CAUSE my Graves' because I had the disease before I started smoking. But now that I have learned about how cadmium accumulates in the tissues, and how cadmium poisoning can accumulate slowly over time..... well, I may need to re-think that one.

And I've avoided all forms of seaweed, which bind to cadmium and remove it from the body. Maybe cadmium overload may be one of the reasons I can't sustain remission.... I learn so much more EVERY DAY!

This article first appeared in the

by Al Adrian

[Chlorella](#) is a green, fresh water algae widely distributed throughout the biosphere, and which possesses unique nutritional properties. Used in Japan since its culture became commercially and technically feasible in the early 60s, chlorella is now Japan's most popular food supplement with over 1,000 tons produced annually.

Chlorella has many interesting nutritional properties. It contains more chlorophyll per gram than any other plant. For comparison, Spirulina contains 7.6 gm of chlorophyll per kilogram, whereas Chlorella contains 20-25 gm per kilogram. In addition, dehydrated Chlorella powder is from 50 to 60 percent protein, and is a significant source of beta-carotene, RNA, and vitamin B-12 (nearly 1.5 times that found in beef liver and therefore an excellent supplement for vegetarians). Chlorella powder also contains vitamin C, vitamin B-1, vitamin B-2, vitamin B-3, vitamin B-5, vitamin B-6, folic acid, and biotin.

However, the real benefit of Chlorella does not lie in consumption of traditionally well defined nutrients such as protein and the B vitamins from a novel source, but rather in consumption of a product which has been shown to have antiviral, wound-regenerating, immune-enhancing, and detoxification properties. Japanese biochemists have isolated an ill-defined water soluble extract of

Chlorella (perhaps peptides) dubbed CGF or Chlorella Growth Factor. Studies in Japan have found CGF to have anti cancer effects in standard cancer rodent models. Furthermore, tests of an acidic polysaccharide extract of Chlorella cell walls have demonstrated interferon induction both in-vitro and in-vivo, and this material intra-peritoneally has been used to produce substantial protection of mice to surgically implanted tumors and infection with influenza virus. This effect on interferon production probably accounts for a 1966 Japanese study which found that two grams of daily chlorella consumption reduced the frequency of colds by 26.5%.

Chlorophyll, well known for its function in photosynthesis in plants, has also been researched for its healing properties in humans. Chlorophyll and chlorella have been found to stimulate the regeneration of tissues. This effect has been studied and exploited in the treatment of a variety of wounds and ulcerative conditions. Topical or oral administration of Chlorella has been found to be useful in the treatment of diabetic skin ulcers, pyorrhea, cervicitis, radiation burns, and pancreatitis. The mechanism by which chlorella speeds healing is under investigation, but it is hypothesized that cell wall polysaccharides stimulate interferon production, this in turn stimulates TNF (tumor necrosis factor) which activates fibroblast activity. This, along with inhibition of proteases released during inflammation results in a synergistic effect on the healing process.

Lastly, but perhaps most importantly, is Chlorella's growing reputation as a dietary detoxification agent. Chlorella's detoxification capabilities have been extensively studied in Japan where it has been found to increase excretion of cadmium from people suffering from "Itai-itai" (cadmium poisoning). Aside from Chlorella's detoxification of heavy metals such as cadmium, uranium and lead, Chlorella cell wall material has also been found to reduce substantially the half-life of synthetically produced hydrocarbons such as PCBs (polychlorinated biphenyls) and chlordane (a pesticide) in rats under experimental conditions. Dr. Ueda of the Kitakyushu City Institute for Environmental Pollution Research in Japan prescribes a daily consumption of four to six grams of chlorella powder in the event of PCB (polychlorinated biphenyls) poisoning—he reports success with the use of this protocol in almost all of those treated.

The [Chlorella](#) product VRP is introducing has been approved for use in Japan for many years and has some unique advantages. Grown indoors under controlled conditions, VRP's chlorella is free of the filth, contaminating microorganisms, insect larvae and pesticides often found in the cultures of species of chlorella grown outdoors. Also, this particular species of Chlorella, *C. chlorella regularis*, yields a digestibility value often exceeding 75%.

In conclusion, although research on the health benefits of chlorella is on-going, and its mechanisms of action are still not completely understood, supplementation with Chlorella on a daily basis is safe and well tolerated (some cases of allergy have been reported). With daily production of pesticides and other synthetically produced chemicals increasing (with accumulation of these substances at the top of the food chain), daily Chlorella supplementation should be of increasing interest to the health conscious consumer.

The following study about cadmium toxicity talks about the disease Itai-Itai, which is a disease of cadmium toxicity characterized by osteoporosis.

Toxicol Appl Pharmacol 2000 May 1;164(3):264-72

Uncoupling between bone formation and resorption in ovariectomized rats with chronic cadmium exposure.

Uriu K, Morimoto I, Kai K, Okazaki Y, Okada Y, Qie YL, Okimoto N, Kaizu K, Nakamura T, Eto S

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[Medline record in process]

Osteoporosis, osteomalacia, and pathological fractures are characteristic features of Itai-Itai disease. The mechanisms of bone damage caused by cadmium (Cd) exposure have not been fully clarified. We investigated skeletal changes in ovariectomized rats with chronic Cd exposure, using bone histomorphometry and mechanical tests. Female Sprague-Dawley rats at the age of 8 weeks were ovariectomized. Eight weeks after ovariectomy, the rats were divided into two groups: Cd-OVX group (n = 15), ovariectomized rats given cadmium chloride (CdCl₂, 0.18 mg/rat) ip three times a week for 28 weeks; Cont-OVX group (n = 10), ovariectomized rats given distilled water alone for 28 weeks. Cd-OVX rats had a significant increase in serum concentration of intact osteocalcin and showed numerical but not significant increase in urinary excretion of

deoxypyridinoline despite a significant decrease in glomerular filtration rate to 40% of the value in Cont-OVX rats. Bone mineral content (BMC) and density were significantly decreased in both the lumbar vertebral body and femur of Cd-OVX rats. Ultimate compressive load in the lumbar body and bending load in the midfemur were significantly lower in Cd-OVX rats than in Cont-OVX rats but the differences were not demonstrated when the values were corrected for BMC. Structural moduli in the lumbar vertebral body and the midfemur were not different between the two groups. Cd-OVX rats showed significant decreases in the trabecular bone volume and trabecular number with increased values in the indices of bone formation and resorption in the lumbar vertebral body cancellous bone in comparison with Cont-OVX rats. In the midfemur, Cd-OVX rats had significantly smaller cortical bone area than Cont-OVX rats but the moment of inertia was identical between the two groups. The indices of bone formation and resorption at endocortical surface of the midfemur were significantly increased in Cd-OVX rats over those in Cont-OVX rats, whereas the indices of bone formation at the periosteal surface were not different between the two groups. These data suggested that chronic Cd exposure exacerbated the uncoupling between bone formation and resorption in ovariectomized rats, which resulted in the osteopenia, structural changes of the bone, and decreased mechanical strength in ovariectomized rats with chronic Cd exposure. Copyright 2000 Academic Press.

The following study makes me wonder if the ear ringing experienced in thyroid disease is related to cadmium toxicity.

Hear Res 1999 Mar;129(1-2):61-70

The effect of combined administration of cadmium and furosemide on auditory function in the rat.

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A number of heavy metals have been associated with toxic effects to the peripheral or central auditory system. These include lead, arsenic, mercury, platinum and organic tin compounds. In addition, the ototoxic effects of some metals may be potentiated by other factors. However, the auditory effects of cadmium have not previously been reported. The purpose of the present study was to investigate the potential ototoxic effects of cadmium from an acute dosage, and its potentiation by furosemide. Auditory brainstem response (ABR) thresholds were measured in adult Sprague-Dawley rats. Rats received either cadmium chloride (5 mg/kg, i.p.) followed by saline (4 ml/kg, i.p.), cadmium chloride followed by furosemide (200 mg/kg, i.p.), or furosemide alone. Follow-up ABRs were carried out 7 days post-treatment and threshold changes were compared between each treatment group. No significant threshold change was seen for the cadmium chloride plus saline treated or the furosemide treated animals. However, significant threshold elevations were observed in animals receiving cadmium chloride plus furosemide. In addition, scanning electron microscopy revealed extensive hair cell loss in animals treated with cadmium chloride and furosemide. Although functional auditory changes were not seen after the administration of cadmium alone, the potentiation of threshold changes by furosemide suggests that cadmium may be ototoxic under certain conditions.

The following study shows that cadmium has a stronger effect in inducing selenium and vitamin E deficiencies than 11 other minerals.

Am J Vet Res 1982 May;43(5):851-7

Amounts of twelve elements required to induce selenium-vitamin E deficiency in ducklings.

Van Vleet JF

Mortality and myopathy of selenium-vitamin E (Se-E) deficiency was produced, in a concentration-dependent pattern, during a 4-week study of 750 ducklings fed a commercial duck starter mash that contained adequate amounts of Se and E, and supplemented with multiple amounts of Ag (50 to 3,000 mg/kg of feed, as acetate), Zn (3,000 to 6,000 mg/kg, as sulfate), Cd (10 to 500 mg/kg, as sulfate), Te (25-500 mg/kg, as tetrachloride), Co (100 to 1,000 mg/kg, as chloride), Cu (500 to 1,500 mg/kg, as sulfate), Hg (200 to 400 mg/kg, as chloride), and Sn (1,000 mg/kg, as chloride). Also, feeding supplements of Pb (500 mg/kg, as acetate), As (600 mg/kg, as sodium arsenilate), Fe (5,000 mg/kg, as sulfate), and S (5,000 mg/kg, as sodium sulfite) produced a low-to-medium frequency of lesions of Se-E deficiency. In ducklings with muscle lesions, the gizzard was most often affected (84.2%), followed in decreasing order by skeletal muscles (69.7%), intestine (34.9%), and heart (23.0%). The frequency of skeletal muscle lesions was high in birds fed Ag, and myocardial necrosis was frequent in ducklings fed Te and Hg. Ducklings affected with myopathy were reluctant to stand. Subcutaneous edema, with or without hemorrhages, and pale areas of myonecrosis in gizzard, skeletal muscles, intestine, and heart were seen at necropsy. Birds fed Te and Hg often had hydropericardium and hemorrhagic myocardial necrosis. Seemingly, addition of many elements to a Se-E adequate commercial diet will increase the requirement for Se-E. In our duckling model, minimal amounts shown to induce Se-E deficiency were 50 mg of Ag/kg, 3,000 mg of Zn/kg, 10 mg of Cd/kg, 25 mg of Te/kg, 1200 mg of Co/kg, 500 mg of Cu/kg, 200 mg of Hg/kg, 1,000 mg of Sn/kg, 500 mg of Pb/kg, 600 mg of As/kg, 5,000 mg of Fe/kg, and 5,000 mg of

S/kg.

The following study shows that cadmium accumulates in the thyroid more than most other areas of the body. Perhaps this indicates that cadmium has a role in thyroid function.

Environ Res 2000 Nov;84(3):211-8

Mercury, selenium, and cadmium in human autopsy samples from Idrija residents and mercury mine workers.

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[Medline record in process]

Total Hg and Se concentrations were determined in autopsy samples of retired Idrija mercury mine workers, Idrija residents living in a Hg-contaminated environment, and a control group with no known Hg exposure from the environment. In selected samples we also checked the presence of MeHg. The highest Hg concentrations were found in endocrine glands and kidney cortex, regardless of the group. MeHg contributed only to a negligible degree to the total mercury concentrations in all analyzed samples. In the Hg-exposed groups the coaccumulation and retention of mercury and selenium was confirmed. Selenium coaccumulation with a Hg/Se molar ratio near 1 or higher was notable only in those tissue samples (thyroid, pituitary, kidney cortex, nucleus dentatus) where the mercury concentrations were $>1 \text{ } \mu\text{g/g}$. After tissue separation of such samples the majority of these elements were found in the cell pellet. Because the general population is continuously exposed to Cd and possibly also to Pb from water, food, and/or air, in some samples the levels of these elements were also followed. In all examined control tissue samples the average values of Cd (kidney cortex, thyroid, hippocampus, cortex cerebellum, nucleus dentatus) and Pb (thyroid, hippocampus) exceeded the average values of Hg. **Cd concentrations were the highest, particularly in kidney cortex and thyroids** ($\mu\text{g/g}$), but no relationship between Cd and Se concentration was evident at the tissue level. Regarding the results in the control group, it is debatable which element is the more hazardous for the general population as concerns neurotoxicity. Copyright 2000 Academic Press.

J Environ Pathol Toxicol Oncol 2000;19(3):201-13

Oxidative mechanisms in the toxicity of chromium and cadmium ions.

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Chromium and cadmium are widely used industrial chemicals. The toxicities associated with both metal ions are well known. However, less information is available concerning the mechanisms of toxicity. The results of in vitro and in vivo studies demonstrate that both cations induce an oxidative stress that results in oxidative deterioration of biological macromolecules. However, different mechanisms are involved in the production of the oxidative stress by chromium and cadmium. Chromium undergoes redox cycling, while cadmium depletes glutathione and protein-bound sulfhydryl groups, resulting in enhanced production of reactive oxygen species such as superoxide ion, hydroxyl radicals, and hydrogen peroxide. These reactive oxygen species result in increased lipid peroxidation, enhanced excretion of urinary lipid metabolites, modulation of intracellular oxidized states, DNA damage, membrane damage, altered gene expression, and apoptosis. Enhanced production of nuclear factor-kappaB and activation of protein kinase C occur. Furthermore, the p53 tumor suppressor gene is involved in the cascade of events associated with the toxicities of these cations. In summary, the results clearly indicate that although different mechanisms lead to the production of reactive oxygen species by chromium and cadmium, similar subsequent mechanisms and types of oxidative tissue damage are involved in the overall toxicities.

The following study seems to indicate that cadmium causes iron deficiency anemia.

Jpn J Vet Res 2000 May;48(1):15-28

Experimental reproduction of itai-itai disease, a chronic cadmium poisoning of humans, in rats and monkeys.

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To establish a useful animal model of Itai-Itai disease (IID) of humans, we conducted the following experiments. Experiment 1: Toxic effects of Cd were compared between ovariectomized (OX) and non-OX rats after daily, intravenous injection of cadmium (Cd) chloride for 14 days. In this experiment, we

demonstrated that OX rats were more susceptible to Cd-induced nephrotoxicity and hepatotoxicity than non-OX rats. Experiment 2: OX rats were injected with Cd at doses of 1.0 and 2.0 mg/kg, 5 days a week, for 13 weeks. The bone Cd content was gradually increased for 13 weeks in a dose-dependent manner. Calcium and phosphorus contents in the bone and serum levels of parathyroid hormone and osteocalcin were not significantly different between Cd-treated and control rats. Mild osteomalacic lesions in the cortical bones of the midshaft haversian canals as well as chronic nephropathy appeared in the rats of the 2.0 mg/kg group. Experiment 3: OX rats were treated with Cd at doses of 0.5 and 0.05 mg/kg for 70 weeks. The rats of the 0.05 mg/kg group showed slight anemia and mild degeneration of tubular epithelium after 50 weeks of treatment. In the 0.5 mg/kg group, the rats showed definite osteomalacia of bones and nephrosclerosis. The Cd concentration in the bones increased for the first 25 weeks, but was replaced gradually with iron at from 50 to 70 weeks of the administration period. Iron deficiency anemia appeared in the 0.5 mg/kg group at from 12 to 25 weeks, and changed to renal anemia after 50 weeks of administration. The anemia at 50 and 70 weeks was normocytic and normochromic, and serum erythropoietin levels were not elevated in response to the decrease of hemoglobin concentrations of red blood cells. Experiment 4: Ten, OX cynomolgus monkeys were given intravenous injections of 0, 1.0 or 2.5 mg/kg/day Cd, 2 or 3 days per week, for 13 to 15 months. Normocytic and normochromic anemia, renal lesions characterized by tubular atrophy and interstitial fibrosis (Cd nephropathy), and bone lesions characterized by an increase of osteoid and osteopenia (Cd osteopathy) were induced in the monkeys treated with Cd. These results demonstrated that chronic cadmium toxicosis similar to IID of humans was reproducible in rats and monkeys by repeated intravenous injection of Cd and that a disease entity closely resembling IID of humans could be induced in experimental animals by chronic Cd toxicosis without participation of malnutrition, vitamin D deficiency, impaired absorption at the intestinal mucosa or multiparous birth.

Med Hypotheses 1985 Jul;17(3):231-42

Zinc, cadmium, metallothionein, and progesterone: do they participate in the etiology of pregnancy induced hypertension?

Chisolm JC, Handorf CR.

Cadmium, a toxic heavy metal, has been incriminated in the etiology of essential hypertension. Zinc, an essential micronutrient necessary for growth, competes with cadmium for binding sites in biochemical processes; zinc deficiency states (i.e. pregnancy and low protein diet) might expose an individual to increased risk of cadmium toxicity. The increased sensitivity to cadmium during pregnancy could also be related to the effect of progesterone on zinc and cadmium metabolism through the actions of metallothionein (MT). MT is a low molecular weight protein believed to function in cadmium detoxification. Several studies in lab animals have documented a late gestation drop of maternal MT levels. This was thought to be due to rising progesterone levels. If there is also a late gestation drop in human maternal MT, then the propensity toward maternal cadmium toxicity would be enhanced. Therefore, we propose that when a zinc deficient woman becomes pregnant and is exposed to both the nutritional demands of the fetus and to the influence of progesterone, she will be likely to develop the manifestations of cadmium toxicity (i.e. hypertension, proteinuria, edema, etc.).

If it is common that members of the brassica family show high cadmium levels, is cadmium the reason why brassicas are goitrogenic?

Plant Physiol 1995 Dec;109(4):1427-1433

Mechanisms of Cadmium Mobility and Accumulation in Indian Mustard.

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Indian mustard (*Brassica juncea* L.), a high biomass crop plant, accumulated substantial amounts of cadmium, with bioaccumulation coefficients (concentration of Cd in dry plant tissue/concentration in solution) of up to 1100 in shoots and 6700 in roots at nonphytotoxic concentrations of Cd (0.1 [μg]/mL) in solution. This was associated with a rapid accumulation of phytochelatin in the root, where the majority of the Cd was coordinated with sulfur ligands, probably as a Cd-S₄ complex, as demonstrated by x-ray absorption spectroscopy. In contrast, Cd moving in the xylem sap was coordinated predominantly with oxygen or nitrogen ligands. Cd concentrations in the xylem sap and the rate of Cd accumulation in the leaves displayed similar saturation kinetics, suggesting that the process of Cd transport from solution through the root and into the xylem is mediated by a saturable transport system(s). However, Cd translocation to the shoot appeared to be driven by transpiration, since ABA dramatically reduced Cd accumulation in leaves. Within leaves, Cd was preferentially accumulated in trichomes on the leaf surface, and this may be a possible detoxification mechanism.

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CADMIUM SOURCES

Following is a remarkable chapter from Henry Schroeder's book about toxic metals. We have seen that cadmium is a principal toxic metal which disturbs zinc, copper, and other metals and probably is a major contributor to thyroid disease. Avoiding cadmium is essential to preserve zinc and copper and normal thyroid function.

All of the tables mentioned are not in yet, but the one that is shows that cadmium can come from many sources that we are exposed to: tobacco smoke, burning oil, automobile tire dust, cadmium batteries, canned foods, dried foods, cola drinks, processed coffee, decaffeinated coffee, milk (from galvanized dairy cans, butter, olive oil, lipstick, silver polish residue on eating utensils, metal ice trays, processed meats, pottery, plastic wrappings, wheat gluten, the electric elements that are put directly into containers to heat water for soups, teas, and coffees, and many other sources. Many of these foods have come under scrutiny and perhaps the reason that they bother people is the cadmium content.

Take some time and read this very important document.

CADMIUM, THE DRAGON'S TEETH

From: *The Poisons Around Us, Toxic Metals in Food, Air, and Water*
by Henry A. Schroeder, M.D. (Published about 1974)

Doctors concerned with occupational diseases have long known that cadmium is poisonous. Pharmacologists, also, have known that small doses lead to bizarre effects in animals. At the turn of the century, cadmium was a rather rare metal nearly always associated with zinc, little used industrially, a metallic curiosity with a bluish-white luster quite impervious to corrosion, like tin.

World War I brought enormous demands for tinned food and a shortage of tin, so that a substitute was needed. Cadmium was ideal though expensive, but its possible toxicity in foods required investigation. In the early twenties, a deluge of literature appeared showing that cadmium was not suitable for coating food containers; small amounts dissolved by acid foods and drinks made animals and people acutely ill.

The reader may remember the old Greek myth about Europa, daughter of the King of Phoenicia, who was abducted by a traveling bull and from whom Europe gets its name. Cadmus, her brother, was sent by his father to find her. Cadmus consulted the Delphic oracle and was commanded to give up the search, for Zeus had the lady in Crete for his own amorous purposes. Instead, he was told to follow a certain traveling cow and to build a town where the cow sank down exhausted. He chased the cow through two countries and built the citadel of Thebes where she sank. Cadmus then sent some people to fetch water from the well of Ares, which was guarded by an unfriendly dragon. The dragon slew them, as that was his job. Cadmus killed the dragon, and on the advice of Athena, ploughed a field and sowed the dragon's teeth. A regiment of fully armed fighting men sprang from the ground, charged, and turned on each other until all but five were killed. These five were the first Thebans, the Sparti, or sown-men.

Cadmium has somewhat the same properties as the dragon's teeth. It looks innocuous but it has a vast potential to poison. Unlike the sown-men, it is not recognizable as an enemy, acting subtly and undercover, mimicking diseases in man for which other causes have been proposed, accumulating in the body slowly until "the threshold of resistance is overcome, then striking. This subtle property was not recognized until recently.

With the loss of Malayan tin in World War II, cadmium was again considered as a substitute for tin cans. As a result, another spate of papers appeared in the middle forties again showing its animal toxicity. The memory of Science is often short.

In spite of its toxicity, cadmium was used to coat ice trays in electric refrigerators. Some people like to make lime or lemon sherbets by freezing the mixes in ice trays. The acid will dissolve some cadmium, and in the mid-thirties there were several cases of acute cadmium poisoning with a few deaths from this source. Dr. Thomas Arthur Gonzales, then assistant medical examiner of New York City, tracked it down, and cadmium-coated ice trays were banned in New York. (But not everywhere. In the late fifties, I discovered four such trays in my General Electric refrigerator and banned them.)

Dr. Gonzales, being a thorough scientist, analyzed the organs of his cadmium victims by the method then available. He found the kidneys loaded with cadmium but so were the kidneys of people dying of other causes. He gave up the study, and it was not until 1953 that Dr. Isabel H. Tipton found much but

varying-amounts of cadmium in kidneys of all the adult Americans she examined, but little or none in babies' kidneys, thus starting us on our worldwide search for cadmium and its sources.

Cadmium became well established as an anticorrosive plating on metal parts during World War II. It was virtually essential for aircraft exposed to salt spray, and hardened aluminum nuts, bolts, cylinders, small parts, and valves showed the characteristic pale yellow color of cadmium plating. In 1944 I took a hundred gravity-operated valves, part of automatic equipment for pilots' anti-blackout suits, on an aircraft carrier far into the Pacific Ocean for three weeks. They lasted two weeks under operating conditions. When similar valves were anodized with cadmium, not a single one out of some fifty thousand failed from corrosion. Nor has one failed since.

Thus, cadmium is replacing zinc as a plating on metal. Some 16,000 tons are used yearly and consumption rises every year. In New York City alone, there are 152 small companies engaged in cadmium plating. Metal parts are put into an electrolytic bath containing cadmium salts, plated, and then removed and washed off with fresh water. The drippings go down the drain. The cadmium enters the city's sewage treatment plants, collects, and in time poisons the bacteria digesting sewage and garbage. The treatment plant then has to shut down for several months, in the interim discharging raw sewage into the rivers and the harbor. Not only is raw sewage an unpleasant pollutant, but the cadmium precipitates in salt water to the bottom mud, where it can enter the food chain. Just a little cadmium, a half to one part per million in water, is toxic to most bacteria tested.

Two lawsuits have been brought by the U.S. Department of Justice. One is against the City of New York, the mayor, his environmental protection administrator, his water commissioner, and two electroplaters as representatives of a class of about 200 firms for polluting federal waterways with cadmium, other heavy metals, and toxic substances. The second is against the State of New Jersey and its many towns and cities discharging into the Hudson River and New York Harbor. These suits demand compliance with city, state, and federal regulations on pollution of the aquatic environment with antimony, arsenic, barium, boron, bromine, cadmium, chromium, copper, fluoride, gold, iron, lead, manganese, magnesium, mercury, molybdenum, nickel, rhodium, selenium, silver, thallium, titanium, tungsten, vanadium, and zinc (see Table VII-1).

If the Department of Justice wins, and discharge of cadmium into sewers virtually ceases, it will still be too late for the fish in the Hudson River. The Trace Element Laboratory and the Environmental Protection Agency have evidence that over half the fish in the Hudson River are unsafe to eat regularly because of contamination with cadmium.

One cannot predict how much cadmium is in fish by measuring it in water. The Hudson River has very little cadmium dissolved in it, a few (3-6) parts per billion, but its fish have a good deal. Four Alabama rivers had 6, 12, 65, and 90 parts per billion cadmium, respectively; about the same amount of cadmium, very little, was found in fish from these rivers (Table VII-2). Compare these Alabama fish with Hudson River fish and the difference becomes obvious. The Hudson River cadmium is in the mud and the food chain; in the Alabama rivers cadmium is in the water and in the mud at the source but not downstream. It is cadmium in mud, not in water, that we must worry about.

In 1972, a lawsuit by the Department of Justice against the Marathon Battery Company and Sonotone Corporation was won by consent of the defendants. These companies made cadmium-nickel batteries for warplanes, hearing aids, power tools, and electric shavers and were discharging wastes into Foundry Cove on the Hudson River. Mr. David M. Seymour, a worker for the Audubon Society, and Robert H. Boyle, a free-lance writer on sport fishing, were walking by the cove and noticed that the mud had a greenish gray color, like pea soup. They sent us some of the mud and Alexis P. Nason, our laboratory analyst, found that it contained over 16% cadmium and 22% nickel. There were an estimated 25 tons of cadmium and 32 tons of nickel in the cove, which at \$2.00 and 80 cents a pound, respectively, were worth about \$150,000. They asked me what to do. "Mine it" I answered. But they didn't. They began catching fish and sending them to us until Mr. Nason was piled high with work.

About then, Senator Philip S. Hart entered the picture, and his people persuaded us to analyze the 44 Alabama fish listed in the table. Our freezers were full of fish. Mr. Nason analyzed them and said, "No more. The law of diminishing returns is now operative." We had learned most of what we wanted-and needed-to know: cadmium in river water was not necessarily reflected in its fish.

The Department of Justice then entered the fray, and persuaded the **EPA** to do the analyses. Which they did, on everything. It added little to the case, except to show that most Hudson River fish were contaminated, as was the food chain (which we knew).

In December 1971 our laboratory was turned into a miniature courtroom, with lawyers for the prosecution and defense, federal court reporter, oaths, and all the works but a judge. Transcription of my testimony was three inches thick, and so garbled that I never got around to correcting it. But it was enough. The next June the **EPA** announced the verdict: we, who helped discover the stuff, did not even get honorable mention. But the defendants removed most of the cadmium and nickel from Foundry Cove, thus preventing a hundred years of further contamination of the Hudson River. Fortunately, there is yet no cadmium lobby or propaganda institute.

The Hudson River is a local and regional problem. So is the Jintzu River in Japan. A large lead and zinc smelter was discharging its tailings where they were washed by river and rainwater. The river was used for irrigation and drinking by people living downstream. Cadmium and lead entered rice and wheat crops, fish, and people. They accumulated. After many years, a disease named itai-itai --ouch-ouch-- appeared in women past the menopause. Calcium was lost from bones, and they fractured easily. Kidneys were badly damaged. Deformities were severe. Many died. The victims' organs were loaded with cadmium and lead. Even their bones had much cadmium, and cadmium does not usually enter bone. It will probably take a hundred years for that soil and river bottom to cleanse itself of lead and cadmium.

All that happened from a zinc smelter. Cadmium is constantly present in zinc, even the purest. The U.S. Bureau of Standards' standard zinc slab has 0.53% cadmium. The zinc used for galvanizing iron--tin roofs, pails, water storage tanks, iron pipes, gutters, water-softening tanks, maple-sap buckets, cauldrons, barbed wire, chicken fences, wire fences, animal cages, nails, and a host of other articles of iron or steel--is far from pure, generally being the cheapest grade, which contains even more cadmium. Impure zinc can contain up to 2%.

Whenever a slightly acid liquid comes in contact for a time with galvanized metal it dissolves some zinc and cadmium. Rainwater is slightly acid from the dissolved carbon dioxide in the air. Falling on a tin roof, collected by a gutter, stored in a galvanized iron cistern, rainwater will contain zinc and cadmium, for it is slightly corrosive. Soft water is also corrosive, and when it stands overnight in galvanized iron pipes, it dissolves zinc and cadmium. When you draw water for your morning coffee before flushing the pipes by running the water, the cadmium is in the coffee. Most of the galvanized iron plumbing in the old houses of our town has been replaced with copper, for our soft acid water has corroded the pipes. First the zinc and cadmium plating goes, then the iron, which makes the water rusty, and then a leak springs and there is a hurried call to the plumber. Soft water also corrodes copper from pipes--bluish green stains on the toilet bowl and the bath tub are characteristic. Hard water is usually not corrosive. Hot water is much more corrosive than cold.

A number of cases of so-called zinc poisoning have been caused by drinking lemonade which has stood for several hours in galvanized pails, cauldrons, or washtubs. Actually they were due to cadmium poisoning, for zinc is not poisonous except in huge doses. Zinc is necessary for all living things, and plants and animals grow poorly or die when there is not enough zinc in their environments. In zinc-deficient soil, a half dozen galvanized nails driven into the trunk of a fruit tree make the difference between health and disease; a string of barbed wire can make healthy crops grow near the fence. Zinc-deficient chickens can get enough zinc by pecking at the wire on their cages or pens. So can rats by licking galvanized wire. But they also get the cadmium.

The human body contains about 2.2 grams of zinc, and there are mechanisms which keep this amount constant throughout life, unless the diet is low in zinc. The body contains a variable amount of cadmium, normally 30 milligrams in Western society, as little as 10 milligrams or less in certain African nations, as much as 50 or 60 milligrams in some people, especially the Japanese, who have more than the Europeans. Zinc does not accumulate. Cadmium, once in the body, stays, probably for life, in the kidneys, the liver, and the blood vessels. As little as 2 micrograms daily absorbed and retained results in a body burden of 30 milligrams in 40 years. Cadmium displaces zinc but does not act beneficially like zinc; quite the opposite. The human kidney contains 8 to 10 times as much cadmium as do the kidneys of any other mammal, except those pets exposed as we are.

Where does the cadmium come from? The air of some cities contains cadmium from fumes spewed out by zinc smelters and refiners and copper smelters. More than 2,000,000 lb (about 1,000,000 kg) are released into the air space of U. S. cities annually from this source alone. An additional 2,300,000 lb went up the chimney in 1968 from the recovery of scrap metal, and another 300,000 lb from incinerators. World consumption is 31 million lb, of which the U. S. uses 12 to 13 million lb. When we swallow cadmium, only a small amount is absorbed into the body from the gut, perhaps 10%, most of which is excreted in the urine. When we breathe cadmium, we retain about half of it, absorbing it from

the lungs. A pack of cigarettes contains 16-24 micrograms of cadmium, and a smoker can contaminate a whole roomful of people.

Rubber tires, plastics, pigments, plated ware, alloys, insecticides, and solders are some of the things containing cadmium. Some foods have a lot of cadmium, relatively: oysters, foods contaminated in the processing, some instant coffees and teas, some canned foods, kidneys of pigs given cadmium as a worm killer, gelatin and fish dried on chicken wire, some cola drinks. We used to get it from dental fillings, but we don't any more. Pigments can be a source, for cadmium yellow and cadmium red are fast colors; some French lipsticks have it. A necklace of candy "Luv" beads made in Hong Kong was colored with cadmium; it made one little girl sick for over a year and poisoned her brother for a short time.

Cadmium is so ubiquitous in our civilization that it is very difficult to avoid it. Our laboratory developed a diet for rats and mice which is very low in cadmium, so low in fact, that it does not accumulate in their bodies over a lifetime. But we have to keep our animals in a metal-free laboratory on a remote Vermont hilltop, give them absolutely pure water, and take extensive precautions to avoid contamination. All commercial diets contain too much cadmium for our use.

What is the price we pay for environmental cadmium? High blood pressure is one. And a major one. The earliest sign of subtle cadmium toxicity is elevation of the blood pressure (Table VII-3). The usual upper limit of normal for rats' blood pressure is about 140 millimeters of mercury. With only a trace of cadmium in the diet and with only a trace in the kidneys and liver, it was a bit over 80. When rats were fed a commercial diet containing cadmium and some deposited in their kidneys, their blood pressure was about 110. Not high, but higher. When cadmium was given in drinking water and there was much in the kidneys, liver, and blood vessels, the rats had high blood pressure, with large hearts, thickening of the small arteries of their kidneys, and, in some cases, heart attacks and hemorrhages. They also showed hardening of the arteries.

High blood pressure from cadmium has now been produced in rats, rabbits, and dogs. It is not severe, usually, but is the spitting image in all respects of the kind 23 million Americans have, which promotes heart attacks and strokes. When we look at human kidneys, we find that people who died with high blood pressure had either more cadmium or less zinc in their kidneys than did people who died of other causes. Cadmium had displaced zinc and slightly poisoned some zinc system that controlled blood pressure.

We played a trick on Nature. The laboratory developed a drug which contained zinc but which would chelate--bind, or grab--cadmium where it met cadmium and drop zinc in its place. High blood pressure in rats was cured very quickly; some of the cadmium was removed and some zinc put back. In people, this drug has lowered blood pressure for long periods of time, removing a little cadmium from the right places, probably the blood vessels.

In essence, we reproduced a common human disease in animals by using a common toxic metal, cadmium, cured it by removing the metal, found a similar situation in man, and relieved it in the same way. Although there is little more to do except clean up a few minor pieces of the picture puzzle, it will take ten to fifteen years before the medical profession will accept this novel idea, in spite of the fact that our work has been confirmed by others.

There is a curious phenomenon in this story. The right amount of cadmium over a lifetime causes high blood pressure. Too much cadmium does not. When cadmium accumulates beyond the subtle poisoning stage, the kidneys and the liver are damaged and blood pressure falls. The same effect occurs when cadmium is injected. A little raises blood pressure; a lot lowers it. The Japanese with ouch-ouch disease did not have a high incidence of high blood pressure they were too sick. Workers in cadmium battery factories, who breathe a great deal of cadmium into their lungs, do not necessarily have high blood pressure--they are too poisoned. There are many examples of this kind of effect in medicine--the right dose of digitalis improves a failing circulation, but too much increases failure. Nicotine in small doses stimulates nerves; in larger doses it paralyzes.

Emphysema of the lung is a nasty disease. The little air sacs of the lungs rupture, making larger ones. Breathing becomes labored. High blood pressure in the circulation of the lung appears, straining the heart and leading to heart failure. Emphysema patients also have more cadmium in their kidneys and livers than do well people. Cigarette smoke contains cadmium, and it is tempting to guess that cadmium absorbed directly by the lungs initiates high blood pressure there. Emphysema is common in cadmium workers. Our drug might be of value in treating emphysema.

When fed to breeding rats and mice, cadmium causes severe congenital abnormalities, to such extent that the strain dies out. When injected into pregnant rats, it produces toxemia of pregnancy, and into pregnant hamsters, congenital abnormalities in the offspring. Injection is not a fair way to test anything we eat, drink, or breathe, but it serves to show bizarre toxic effects.

Did anyone ever think of injecting waste water from washing machines and dirty dishes into pregnant women? Of course not. Yet that was what the Environmental Protection Agency and the Public Health Service implied when they banned NTA last year.

NTA--nitrilotriacetic acid--like the polyphosphate detergents, is a chelating agent, binding metals. That is its virtue. NTA was allowed as a good substitute for phosphates, which are highly nutritious to plants and cause overgrowth of algae in stagnant lakes, choking off fish life. Some 100 to 125 million tons of NTA were made annually as a substitute. NTA is rapidly biodegradable by oxygen-dependent bacteria, a distinct advantage over phosphates.

Some experiments were done at the National Institute of Environmental Health Sciences--rather rapid ones, I suspect from the data--in which NTA was injected into pregnant rats. No effect. Cadmium and methyl mercury were also injected. No effect. Combined with NTA, cadmium and mercury were both lethal to fetuses and mothers.

The idea is that cadmium and methyl mercury are common water pollutants. NTA gets into the water from drains and combines with methyl mercury and cadmium. Pregnant women drink the water somewhere else and get dead babies. Synergism. The NTA allows the metals to get into the body and pass through the placenta into the fetus.

To anyone with a knowledge of trace metals, there are several glaring flaws in this argument:

1. Although methyl mercury probably occurs in waters where it has been dumped, it has never been demonstrated to exist as such in any water, and it is probably rare in the United States. Regular mercury is found in concentrations of less than 5 parts per billion such small amounts are harmless, NTA or not (Table VII-1).
2. There is a little extra cadmium in some rivers, but most waters have less than 10 ppb, too little to harm a fetus.
3. No one has demonstrated that NTA by mouth increases the absorption of cadmium or methyl mercury by the intestines. Indications are that it doesn't, for most other metal chelates are poorly absorbed--the molecule is too big.
4. Large doses of cadmium and methyl mercury injected into pregnant rats did nothing, although much smaller doses by mouth are bad both for the young and the mothers, as several people have discovered. There was something fishy about the NTA experiments.

Two Swedish technicians came all the way to the Virgin Islands to consult about NTA. They were worried about the data. On critical examination they did not stand up. Neither did the experiments. The Swedes went home satisfied to continue the use of NTA.

The following year the Public Health Service backtracked quietly and lifted the ban on NTA, which is now clean as a hound's tooth, although slightly tarnished in reputation. So it goes.

One of the subtle effects of this product of the dragon's teeth is that no other measurable function of the body is altered, other than the level of blood pressure and what goes with it. The patient does not know that a function of his kidneys detectable only by sophisticated techniques is changed, nor does he feel the difference in his blood pressure, except under anger or anxiety, when he may flush or his heart may pound. Yet his heart works harder with each beat, day and often night, gradually enlarging; the very small arteries of his kidneys constrict in an attempt to protect the delicate capillaries which filter his blood to make urine, and both show signs of strain; he already has a serious blood vessel disease, arteriosclerosis, and the heightened blood pressure increases its progression and makes it worse, both in his large arteries, which do not matter too much, and in the smaller ones of his heart and brain. The process, a vicious cycle, goes on inexorably, until one day in his middle age, there is a sudden accident. An artery in his heart is narrowed to the point where it supplies insufficient blood for the needs of that part of the heart, and he feels the severe pain of angina pectoris. Or the artery plugs, and he has a heart attack, or coronary occlusion. Or, later in life, the same thing happens to an artery in his brain, and he has a stroke or thrombosis. Or an artery in his brain ruptures, and he has a cerebral hemorrhage.

Something like that kills over half the population of our country.

High blood pressure can now be treated with modern drugs and is often reversible, unless it has gone too far. When well-treated, its serious consequences, heart failure and hemorrhage, largely disappear. Unfortunately, it is not as well treated as it should be, even though the death rate from hypertensive heart disease is one quarter of what it was 20 years ago. If we could remove the cadmium from blood vessels, replacing it with needed zinc, regular treatment with drugs could become unnecessary, except at long intervals.

The amount of cadmium we take into our bodies seems to depend on the amount of zinc we also absorb; the more zinc, the less cadmium. We can speculate with reasonable assurance that plenty of zinc may displace a little cadmium in the tissues. We know that animals deprived of cadmium have less zinc in their bodies than do animals fed cadmium, which have twice as much, although they seem healthy. Cadmium demands zinc. Today, with the wide use of refined flour, sugar, and fats, we are not getting enough zinc for our needs, especially if cadmium is around in our food, water, and air. Many Americans, especially teenagers and the aged, have measurable zinc deficiencies.

A major breakthrough in the treatment of poor circulation of the legs resulting from narrowing of the arteries is the use of large amounts of zinc by mouth. Pain ceases, normal color returns, exercise tolerance improves, ulcers and gangrene heal, and the affliction is cured. We don't believe that zinc reverses the arteriosclerosis of the vessels-though it may. Rather we speculate that zinc displaces cadmium and reverses the spasm induced by it in minor arteries. Zinc also works in angina pectoris.

When an artery is narrowed at one point, the small arteries it supplies downstream become highly sensitive to material in the blood which may normally constrict them a little. The end result is marked loss of blood flow. Zinc prevents that sensitivity.

Zinc by mouth is also of value in loss of sense of smell, which can be caused by cadmium, but cause and effect have been established only in cadmium workers. Zinc increases healing of wounds, for it is necessary for the growth of cells. I have also seen it improve tolerance for alcohol, and it has been used with some success in cirrhosis of the liver.

The skeptical reader may ask "Haven't we always had high blood pressure, before cadmium was introduced into the environment?" We have, associated with kidney diseases, at least since 1693, but it has been nowhere near as prevalent as it is now. In certain parts of the world, for example, Burundi, Africa, it occurs only when the kidneys are diseased. The moderate and extremely frequent type seen in this country is only found in civilized societies or in places where there is obvious exposure to cadmium in water--certain islands of the West Indies, where rainwater is collected on galvanized roofs and stored in galvanized cisterns, for example.

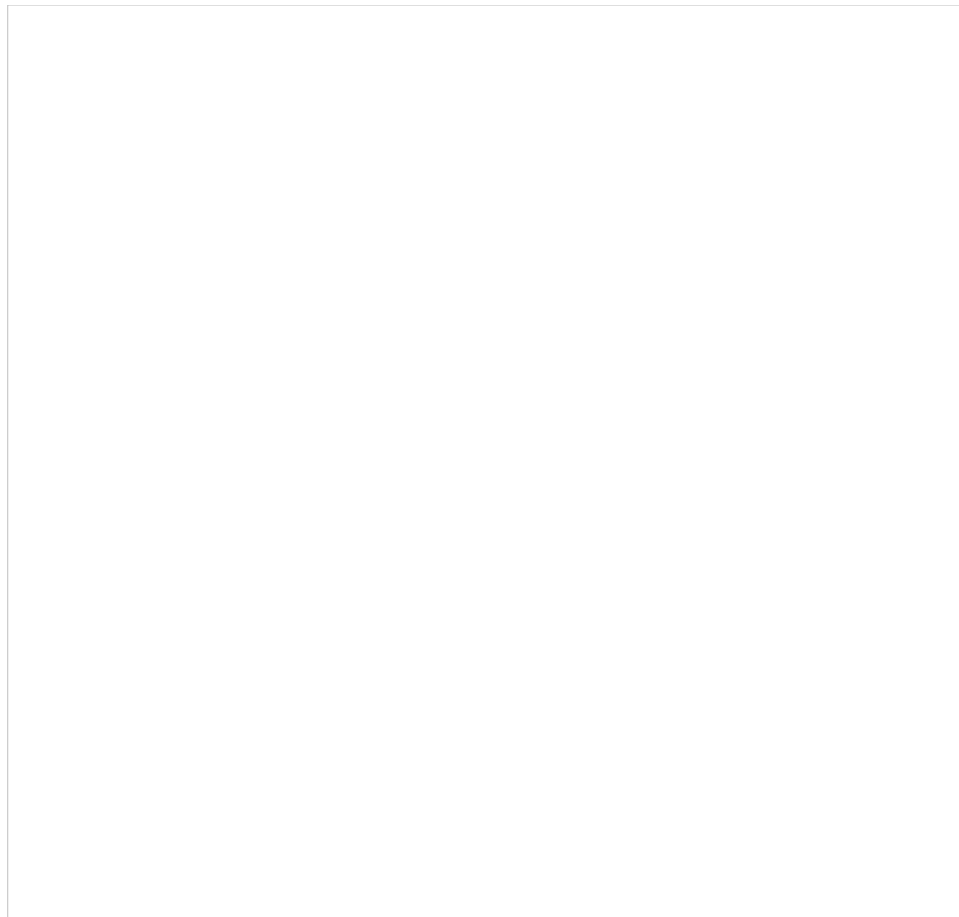
That hypertension is mainly an environmental disease, although it may have a hereditary background, becomes clear when one examines the whole picture. We do not have space for more than the highlights. The Negro race is supposed to be very susceptible to hypertension; in this country, it is, with three or four times as many deaths as among whites. Hypertension is common in West Africa, but not among Central African Negroes. The rate for Negroes is equal to the white incidence in the Virgin Islands but twice as high as the rate for whites in St. Kitts. In other words, the incidence in Negroes varies from negligible to very high depending on the area. The incidence of hypertensive deaths in white people varies from city to city in the U.S. by as much as four times. From country to country it varies by as much as ten times. It is very high in Japan and very low in Thailand. In 94 cities of the United States, the death rate from heart attacks varies directly according to the corrosiveness of finished municipal water (see Table VII-4); in Japan, the death rate from cerebral hemorrhage varies according to the corrosiveness of river water. Death rates from heart diseases vary according to water quality in Britain, Canada, Sweden, the Netherlands, and South America. It is the pipes, and probably cadmium in the pipes, which are responsible.

There is everywhere a marked difference in death rates from heart disease in backward countries between the lowest class and the lower middle class. The first thing a poor family does when it establishes some measure of economic solidarity is to move into a house with running water. There they begin to have heart attacks. Doctors argue that such people eat more fat, or sugar, or what-not, thus accounting for heart disease. Pipes seem more logical villains.

What can we do about the situation with this subtle, accumulative poison, a clear and present hazard to health? First, we can prevent its emission into the air. Whenever zinc is burned or melted there will be

cadmium. Incineration is a major source: burning of automobile tires, red and yellow plastic bags, plastic products, paints, discarded automobiles, discarded airplanes, and the parts thereof. Cadmium pollution can be abated by prevention of air pollution with zinc (Table VII-5).





Second, we can prevent its solution into water--along with lead--by providing municipal waters that are not corrosive. It is not difficult. Almost all municipalities treat their water, but not for corrosiveness.

Third, we can begin to control cadmium entering food and drinks by careful monitoring--by prevention of dumping into rivers and estuaries, by restrictions on its use in food containers--in other words, as we try to control any poison. In Table VU-5 are some examples of foods containing cadmium. Others with more than 1 ppm are smoked kippers, canned anchovies, lamb chops, chicken, olive oil, instant coffees and teas, tea leaves, and caffeine-free coffee; some with more than 0.5 ppm are all seafood, meats, wheat gluten (cadmium goes with the gluten in grains), oils and fats, margarine, Purina Chow, molasses, honey, black pepper, cocoa, butter, and nonfat dried milk, most of them processed.

Although most of the cadmium we encounter comes from food, only small amounts are absorbed by the intestinal tract, and even those are lessened when the diet contains plenty of zinc. It is highly likely that the largest part of the cadmium in our bodies comes from air- from tobacco smoke, polluted air, and dusts--for most of the cadmium inhaled is absorbed directly from the lungs into the body. As little as 1 mcg per day retained would build up a body burden of 14.6 mg in 40 years, over a third of the average amount, 38 mg, in all tissues. A pack of cigarettes contains 20 mcg, of which 10 mcg are absorbed from smoke. So it is easy to get enough cadmium to cause illness.

The pattern of storage of cadmium in the body differs according to the route of entry (Table VII-6). Workers exposed to heavy dusts, as in cadmium-nickel battery plants, had large amounts in their livers, with ratios of concentrations in liver to kidneys usually greater than 1.0. Total amounts stored, of course, were much larger, for the average liver weighs six times as much as the kidneys. Persons with high blood pressure had twice as much cadmium in their kidneys as did normal people, but no more in their livers. Japanese with ouch-ouch disease got their cadmium by mouth, and they actually had less than did those exposed to dusts in factories. The total amount of cadmium stored in the livers and kidneys of exposed workers was nearly 350 mg, the total in those organs of hypertensive persons was only 20 mg, and the total in normal persons was about 12 mg. Therefore, a little cadmium goes a long way.

Cadmium is a perfect example of an accumulative abnormal and subtly toxic trace metal in the environment causing widespread and serious human diseases, most of which are fatal. As such, cadmium is the worst of the bad actors among the metals.

(End of book chapter)

The following study indicates that the particulates in smog may be the critical factor which causes sudden death from heart disease. I believe that there is a very good possibility that these particulates contain cadmium and that cadmium is a major factor causing heart disease and sudden death in persons with pre-existing heart disease. Therefore people with thyroid disease should do their best to avoid smog because of the effects of cadmium on the thyroid.

Smog May Induce Heart Attacks

June 6, 2000

LOS ANGELES (AP) - Smog apparently doesn't hurt just your lungs: New scientific research suggests that even moderate smog may induce sudden death in people with existing heart problems.

The newfound evidence, culled from more than a dozen studies on humans and animals, shows that tiny pieces of soot called particulates may alter the heart rate in some people, the Los Angeles Times reported Monday.

The link has not yet been proven, but there is a strong likelihood that the particles cause the heart problems, possibly indicating air pollution poses a greater public health threat than previously thought, the newspaper said.

Heart disease is the top killer in the United States, responsible for about half of all deaths.

At smog levels found in many U.S. cities, the inhalation of particulates can disrupt a person's ability to regulate the pumping of blood. The threat is particularly severe for older people who have arrhythmia, a condition marked by an irregular heartbeat.

"When particulate pollution increases, the heart rate seems to go up a little bit and the variability in the heart rate seems to go down. Those are things classically seen (in people) with heart failure," said Dr. Timothy Denton, a cardiologist at Cedars-Sinai Medical Center in Los Angeles.

"Studies suggest that people are dying relatively rapidly after you see an increase in particles. Sometimes it's within 24 hours," said Robert Devlin of the Environmental Protection Agency's clinical research branch.

Changes in heart rhythm that occur after breathing particulates are subtle on an electrocardiogram and do not affect healthy people.

Arden Pope, an epidemiologist at Brigham Young University, said "it's incredibly good news" if the link can be proven.

"We already know that about half of us die of cardiopulmonary disease, and if this is true about particulates, we have found a preventable cause," Pope said.

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CALCIUM

Rough file:

"In this paper the authors studied the effects of thyroid hormones and their structural analogues on the mitochondrial calcium transport activities. The thyroid hormones, 3,5,3' L-triiodothyronine (LT3) and 3,5,3',5' L-tetraiodothyronine (LT4) at physiological intracellular concentrations between 7.2 and 9 nM, decouple total Ca⁺⁺ transport, as well as inhibit the passive transport of Ca⁺⁺, either due to oxidation of pyruvate, malate or succinate or after inhibition with rotenone. The optical isomers 3,5,3' D-triiodothyronine (DT3) and 3,5,3',5' D-tetraiodothyronine (DT4) are less effective at all the used concentrations. Furthermore the structural analogues 3,3',5' L-triiodothyronine (LrT3), 3,5-dichloro, 3',5' L-diiodothyronine (LDiCIT2) and 3,5 L-diiodothyronine (LT2) furnished even less effects on the same activities. The effect of the thyroid hormones and of their structural analogues has revealed that the mitochondrial calcium transport may be influenced both by a stereospecific interaction between hormones and protein ligands and by a lipophilic chaotropic action on the mitochondrial membranes lipids. In this context it is interesting to consider that both thyroid hormones and Ca⁺⁺ transport activity are interacting with the energetic metabolism by means of phosphorylation and substrate oxidation mechanism." [calcium--effects on transport by T3.doc](#)

Title

Calcium is the first messenger for the action of thyroid hormone at the level of the plasma membrane: first evidence for an acute effect of thyroid hormone on *calcium* uptake in the heart.

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Segal J

Address

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Source

Endocrinology, 126(5):2693-702 1990 May

Abstract

The thyroid hormone T3 produced a very rapid and transient increase in ⁴⁵calcium uptake by freshly isolated rat heart slices, which was seen already 15 sec after the addition of the hormone, reached a maximum at 30 sec, and then progressively declined and returned to control values after 10 min. This effect of T3 was independent of extracellular *calcium*, concentration related (evident at a physiological concentration of 10 pM, reached maximum of about 75% above control at 1 nM, and was smaller at greater concentrations), and thyroid hormone specific, as judged from the order of potency of several thyroid hormone analogs: L-T3 greater than L-T4 greater than or equal to D-T3 greater than 3'-isopropyl-3,5-L-diiodothyronine greater than D-T4 greater than 3,5-L-diiodothyronine greater than r-L-T3 greater than D,L-thyronine. The inorganic *calcium* channel blockers La³⁺, Cd²⁺, and Mn²⁺ inhibited, in a concentration-related fashion, basal and T3-induced increases in ⁴⁵Ca uptake in the cardiac slices. The organic calcium channel blockers verapamil, nifedipine, and diltiazem were without effect, indicating that in the quiescent cardiac slice the effect of T3 on ⁴⁵Ca uptake is independent of sarcolemmal depolarization. Additional studies demonstrated that the stimulatory effect of T3 on 2-deoxyglucose uptake by the cardiac slices required extracellular *calcium* and was inhibited by the *calcium* channel blockers La³⁺, Cd²⁺, and Mn²⁺. The present study provides conclusive evidence for two central issues: that *calcium* is the first messenger for the prompt, plasma membrane-mediated action of thyroid hormone to increase cellular sugar uptake, and that thyroid hormone produces an acute increase in *calcium* uptake by the heart, an effect that is demonstrable at physiological concentrations and is thyroid hormone specific and, therefore, points to a physiological relevance for this action.

1. Expression of receptors to extracellular *calcium* enables parafollicular cells of the thyroid gland (PF cells) to release calcitonin (CT) and serotonin (5-HT) in response to increased external Ca²⁺. Recently, a *calcium*-sensing receptor (CaR), similar to the G protein-coupled receptor for external Ca²⁺ cloned from parathyroid gland, was shown to be expressed in PF cells. Using a highly purified preparation of sheep PF cells, we have examined the electrical and biochemical processes coupling CaR activation to hormone release. 2. Whole-cell recordings in the permeabilized-patch configuration show that elevated extracellular Ca²⁺ concentration ([Ca²⁺]₀) depolarizes these cells and induces oscillations in membrane potential. In voltage clamp, high [Ca²⁺]₀ activates a cation conductance that underlies the depolarization. This conductance is cation selective, with a reversal potential near -25 mV indicating poor ion selectivity. 3. **The CaR expressed in these cells is activated by other multivalent cations with a rank order potency of Gd³⁺ > Ba²⁺ > Ca²⁺ > > Mg²⁺.** The insensitivity of these cells to high external Mg²⁺ contrasts with the reported sensitivity of the cloned CaR from parathyroid. 4. Elevation of [Ca²⁺]₀ also stimulates increases in intracellular Ca²⁺ concentration ([Ca²⁺]_i) and this effect is largely inhibited by the Ca²⁺ channel blocker nimodipine, indicating that L-type voltage-gated Ca²⁺ channels contribute to the response to elevated [Ca²⁺]₀. 5. Elevated [Ca²⁺]₀ induces an inward current under conditions where the only permeant external cation is Ca²⁺, indicating that influx via the cation conductance is another source of the increases in [Ca²⁺]_i. 6. **Extracellular Ca²⁺ stimulates 5-HT release with an EC₅₀ of 1.5 mM. Nimodipine blocks 90% of the Ca²⁺-induced 5-HT release, while other inhibitors of voltage-gated *calcium* channels had no effect.** These data support an important role for L-type Ca²⁺ channels in CaR-induced hormone secretion. Although earlier studies indicate that high [Ca²⁺]₀ induces release of Ca²⁺ from intracellular stores, thapsigargin-induced depletion of these stores did not affect secretion from these cells, indicating that Ca²⁺ influx is necessary and sufficient for the Ca²⁺-induced 5-HT secretion. 7. Inhibition of protein kinase C (PKC) using chelerythrine, staurosporine, or calphostin C inhibited Ca²⁺-induced 5-HT release by 50% while phorbol ester-induced 5-HT secretion was completely inhibited. Thus, PKC is an important component of the pathway linking CaR activation to hormone release. However, another as yet unknown second messenger also contributes to this pathway. 8. We tested the contribution of two different phospholipases to the CaR responses to determine the source of the PKC activator diacylglycerol (DAG). Selective inhibition of phosphatidylinositol-specific phospholipase C (PI-PLC) with U73122 had no effect on the response to elevated [Ca²⁺]₀. **However, pretreatment with D609, a selective inhibitor of phosphatidylcholine-specific phospholipase C (PC-PLC), inhibited Ca²⁺-induced 5-HT release to 50% of control indicating that phosphatidylcholine is a likely source of DAG in the response of PF cells to elevated [Ca²⁺]** [calcium receptor mediated hormone release.doc](#)

Basal and thyrotrophin (TSH)-stimulated release of iodothyronines (triiodothyronine, T3, and thyroxine, T4) from intact chicken thyroid glands was determined in vitro. In the absence of TSH, T3 and T4 were released in measurable amounts in the incubation media. The release of both

iodothyronines was directly related to the media TSH concentrations and incubation period. Lineweaver-Burke analysis revealed that the V_{max} for T₃ was 99.4 pg/gland, with an apparent K_m of 17.8 mU TSH, and that the V_{max} for T₄ was 323.35 ng/gland, with an apparent K_m of 51.5 mU TSH, demonstrating that T₄ is the major iodothyronine released by avian thyroid glands. **The basal release of T₄ was suppressed by the addition of a calcium chelator (ethyleneglycol-bis-(beta-aminoethylether)-N,N,N',N'-tetraacetic acid; EGTA), a calcium antagonist (cobalt chloride, CoCl₂), or prostaglandin E₁ (PGE₁) to the incubation media.** Basal T₄ released was increased in the presence of a calcium agonist (*lanthanum* chloride, LaCl₃), a calcium ionophore (A23187), dibutyryl cyclic adenosine 3'3'-monophosphate (dbcAMP), isobutylmethylxanthine (IBMX), indomethacin, magnesium chloride (MgCl₂), and potassium iodide (KI). Thyrotrophin-stimulated T₄ release was reduced by CoCl₂, PGE₁, and indomethacin but enhanced by LaCl₃, MgCl₂, and KI. These results demonstrate that it is possible to measure the release of thyroid hormones in an in vitro system in the chicken. Basal and stimulated iodothyronine release from the chicken thyroid gland appears to be mediated by calcium- and cAMP-dependent mechanisms.[calcium antagonists inhibit T4 production.doc](#)

Low bone mineral density (BMD) and increased bone turnover are common features of untreated hyperthyroidism in adult patients. The effect of treatment on BMD is still controversial. BMD and bone metabolism in hyperthyroid children have not been thoroughly investigated. In the present study, we measured spinal and whole body BMD by dual-energy X-ray absorptiometry in a group of 13 girls (aged 5.0-14.9 years) at diagnosis of hyperthyroidism. The bone resorption rate was assessed by urine measurement of N-terminal telopeptide of type I collagen (NTX). Hyperthyroid patients have been studied longitudinally during treatment. BMD values and NTX urine concentrations have been also determined in 155 healthy Caucasian girls (aged 2.4-24.2 years). Spinal and whole body bone density measurements were significantly lower compared with healthy controls in untreated hyperthyroid girls, after correction for differences in age and anthropometric measurements ($p \leq 0.033$). Bone density measurements obtained after 12 and 24 months of treatment were no longer different from those of healthy girls. NTX urine levels at diagnosis of thyrotoxicosis were significantly higher than those found in healthy controls ($p < 0.0001$); 6 months after treatment, the urine levels did not show significant differences, and they remained stable after 12 and 24 months of therapy. Inverse correlations at diagnosis were found between serum-free thyroxine (FT₄) serum levels and spinal ($r = -0.42$) and whole body bone density ($r = -0.41$); FT₄ and free triiodothyronine serum levels directly correlated with the NTX concentration ($r = 0.77$, and $r = 0.71$, respectively). In conclusion, the results of the present study demonstrate that low bone density values and high bone resorption rates are found in hyperthyroid children and adolescents at diagnosis of the disease. Our data also demonstrate that antithyroid treatment is able to reduce dramatically the bone resorption and to increase significantly both spinal and total body BMD, granting physiologic conditions for the achievement of the best obtainable peak bone mass.[calcium--bone mineral density increases in hyperT girls during treatment.doc](#)

Calcium may become a dieter's best friend

From Science News, April 29, 2000

There's encouraging news for people who've been losing the battle of the bulge. Weight loss may be at hand-if that hand begins reaching for a glass of milk, slice of cheese, or dish of yogurt, all low-fat, of course.

At the Experimental Biology 2000 meeting last week in San Diego, scientists from the University of Tennessee in Knoxville reported dramatic findings from a weight-loss study in mice. How much calcium the animals consumed-and its source-greatly affected what share of their meals turned to fat.

Reanalysis of data collected earlier on women supports that finding, another scientist adds.

The Tennessee team used mice that model human patterns of obesity. The animals had been genetically engineered to express in their fat cells a gene called *agouti*, which normally operates in human but not mouse fat cells. This gene strongly influences whether a fat cell burns energy-containing molecules or converts them to fat.

Michael B. Zemel, who directs the university's Nutrition Institute, and his colleagues put these mice onto a low-calorie diet for 6 weeks. Their meals contained just 70 percent as much energy as the rodents would normally choose to eat. One group received a diet that was also deficient in calcium. Its calcium content, adjusting for species differences, is "almost exactly what American women are consuming," Zemel notes, "about 500 milligrams per day." That's well below the recommended daily allowance of 1,300 mg calcium.

The calorie-restricted mice lost 8 percent of their body fat and 11 percent of their weight.

Zemel's group again restricted the food but boosted calcium intake of another two groups of the mice. Each received the mouse equivalent of a human dose of 1,600 mg calcium per day. Mice getting this as a carbonate supplement lost 42 percent of their body fat and 19 percent of their weight. Those that consumed the extra calcium as nonfat dry milk-substituted for an equal amount of dietary protein-lost 60 percent of their body fat and 25 percent of their weight.

A fourth group, receiving twice as much dairy-derived calcium, showed little extra benefit, Zemel notes.

These differences occurred even though all of the low-calorie groups got the same exercise and mix of dietary fat, protein, and carbohydrates. The results show that varying dietary calcium alters the animals' metabolism, says Zemel. Among the dieting animals, core body temperatures measure of basal energy use-fell during the low-calcium diet but climbed with the high-calcium chow.

Under low-calcium conditions, the Tennessee scientists find, the *agouti* gene directs calcium channels to open. "That turns out to be a bad thing," Zemel says, because it activates fat synthesis while suppressing fat breakdown.

Zemel's group is now testing whether a 6-month augmentation of dietary calcium will offer similar weight-loss benefits to obese women.

"I'm impressed by this," says Robert Marcus of the Veterans Affairs Medical Center in Palo Alto, Calif., referring to the mouse data reported last week.

When endocrinologist Robert P. Heaney of Creighton University in Omaha, Neb., first learned of preliminary data by Zemel's group last year, "I thought they made sense-but I still had a degree of skepticism," he says. So, he reanalyzed data from five calcium-supplement trials he had conducted in people over the years.

"And in all five," he says, "we found a significant weight effect that we had ignored." These data, to be published soon, show that women consuming the least calcium weighed the most.

Ironically, Zemel says, among weight-conscious teens, "the first thing they jettison from their diet is dairy." This choice, he suspects, is "moving them farther from their goal, not closer." *J. Raloff*

The following is interesting, but I don't know the exact source.

CHAPTER SIXTEEN

CAN CALCIUM CURE CANCER?

In 1932 Otto Warburg won the Nobel Prize in Medicine for his discovery that cancer was anaerobic: cancer occurs in the absence of free oxygen. As innocuous as this discovery might seem, it is actually a startling and significant finding worthy of a Nobel Prize. What it basically means is that cancer is caused by a lack of free oxygen in the body and therefore, whatever causes this to occur is the cause of all cancers.

In chemistry, alkali solutions (pH over 7.0) tend to absorb oxygen, while acids (pH under 7.0) tend to expel oxygen. For example, a mild alkali can absorb over 100 times as much oxygen as a mild acid. Therefore, when the body becomes acidic by dropping below pH 7.0 (note: all body fluids, except for stomach and urine, are supposed to be mildly alkaline at pH 7.4), oxygen is driven out of the body thereby, according to Nobel Prize winner Otto Warburg, inducing cancer. Stomach fluids must remain acidic to digest food and urine must remain acidic to remove wastes from the body. Blood is the exception. Blood must always remain at an alkaline pH 7.4 so that it can retain its oxygen. When adequate mineral consumption is in the diet, the blood is supplied the crucial minerals required to maintain an alkaline pH of 7.4. However when insufficient mineral consumption is in the diet, the body is forced to rob Peter (other body fluids) to pay Paul (the blood). In doing so, it removes crucial minerals, such as calcium, from the saliva, spinal fluids, kidneys, liver, etc., in order to maintain the blood at pH 7.4. This causes the de-mineralized fluids and organs to become acidic and therefore anaerobic, thus inducing not only cancer, but a host of other degenerative diseases, such as heart disease, diabetes, arthritis, lupus, etc..

Everyone knows that the human body is made up of 78% water by weight, and that water is hydrogen and oxygen gases. When nitrogen gas and carbon in the form of carbon dioxide and methane gases are added, the total gas in the body by weight becomes over 95%. Almost half of the remaining 5% that makes up the human body and controls all biological functions is the mineral calcium,

No other mineral is capable of performing as many biological functions as is calcium. Calcium is involved in almost every biological function. This amazing mineral provides the electrical energy for the heart to beat and for all muscle movement. It is the calcium ion that is responsible for feeding every cell. It does this by latching on to seven nutrient molecules and one water molecule and pulls them through the nutrient channel. It then detaches its load and returns to repeat the process. Another important biological job for calcium is DNA replication, which is crucial for maintaining youth and a healthy body. Calcium ions are indispensable for DNA replication (Calcium in the Action of Growth Factors, W.H. Moolenaar, L.K. Defize, and S.W. Delaat, 1986 Calcium and the Cell, Wiley) which is the basis for all body repair. It can only occur "on a substrate of calcium" (The Role of Calcium in Biological Systems, Albert Lehninger, Professor of Medical Science, John Hopkins University, Volume 1, CRC Press). Thus, low calcium means low body repair and premature aging. As important as all these and hundreds of other biological functions of calcium are to human health, none is more important than the job of pH control. Calcium to acid, is like. water to a fire. Calcium quickly destroys oxygen robbing acid in the body fluids. Thus, the more calcium, the more oxygen, and therefore, the less cancer and other degenerative disease.

This information then begs the question, "How much calcium is necessary?" Biologically, the human body requires 800 milligrams daily, but since calcium is extremely difficult for the body to absorb, the question then becomes "How much calcium do we have to consume to absorb 800 milligrams?" As was discussed in previous chapters, the cultures around the world that consume "Milk of the Mountains", the Hunzas in Pakistan, the Armenians, Azerbaijanians and Georgians in Russia, the Vilcabamba Indians in Ecuador, the Titicacas Indians in Peru, the Bamas in China and the 'Iligrams of Tibetans, all actually ingest an astounding 100,000 milligrams of calcium each day, and all have no cancer, diabetes, heart disease, arthritis, and all other degenerative diseases as well as mental disorders. This proves that you cannot consume too much calcium and that excess calcium must readily pass harmlessly out of the body through the urine. The only long living culture that does not consume the "milk of the Mountains" is the Okinawans who consume large quantities of "Milk of the Oceans"

Millions of Okinawans live in the southern coral islands of Japan with the average life expectancy of 105 years, while mainland Japan is just 77 years. The Okinawans live on islands made of coral reefs which are mainly calcium. The Okinawans discovered over 500 years ago that feeding coral sand that is produced from the weathering of the reefs to the chickens and cows results in twice as many eggs and twice as much milk. They also found that when the coral sand is used as a

fertilizer, crops increase by as much as three fold. When they finally, 500 years ago, began to consume the coral sand themselves, all of the under utilized doctors were forced to leave the islands. This was known in Japanese history as the Japanese Exodus.

The early European explorers discovered their secret and hauled shiploads of the calcium rich coral sands back to Europe. In Madrid Spain, the historic monument of the world's first drugstore contains rows of shelves labeled "coral calcium from Okinawa Japan". Today millions of people all over the world consume coral calcium, and as a result, there are millions of medical testimonials.

The phenomenon of preventing and reversing degenerative disease through the consumption of large amounts of mineral and vitamins did not go unnoticed by men of medicine. Hundreds of years ago European doctors were prescribing coral calcium and other nutrients to their patients. In the 1950s, Dr. Carl Reich M.D. discovered that his patients were able to "cure themselves" of almost all degenerative diseases by consuming several times the RDA of calcium, magnesium, vitamin-D and other nutrients. Dr. Reich was the first North American doctor to prescribe "mega doses" of minerals and vitamins to his patients and is considered by many to be the father of preventive medicine. By the 1980s Dr. Reich had cured thousands, but lost his license for explaining that the consumption of mineral nutrients, such as calcium, could prevent cancer and a host of other diseases. This concept was considered "too simple" to accept by the medical wisdom of the day. However, by the late 1990s, other medical men of wisdom were also discovering that calcium supplements could indeed reverse cancer. In the October 13, 1998 issue of the New York Times wrote an article appeared entitled "Calcium Takes Its Place As a Superstar of Nutrients" in which it reports that a study published in the Journal of the American Medical Association reported that "increasing calcium induced normal development of the epithelia cells and might also prevent cancer in such organs as the breast, prostate and pancreas". It also reported that the American Journal of Clinical Nutrition published "virtually no major organ system escapes calcium's influence" and that a research team from the University of Southern California found "adding calcium to the diet lowered the blood pressure in 100 black teenagers". The January 14, 1999 issue of the Phoenix Republic wrote in an article entitled "Calcium Reduces Tumors" that the New England Journal of Medicine reported "adding calcium to the diet can keep you from getting tumors in your large intestine". Then the February, 1999 issue of the Readers Digest wrote in an article entitled "The 'Superstar' Nutrient" that the Journal of the American Medical Association published "when the participants consumption reached 1500 milligrams of calcium a day, cell growth in the colon improved toward normal (this means that the cancer was reversed)". The Digest also reported that the Metabolic Bone Center at St. Lukes Hospital believes that "a chronic deficiency of calcium is largely responsible for premenstrual syndrome (PMS)" and that "a lot of women are avoiding the sun and their vitamin-D levels may be very low". In the same article, the Digest reported that "in 1997 the large federally financed trial found that a diet containing 1200 milligrams of calcium significantly lowered blood pressure in adults". Then the May 3, 1999 edition of US World News Report wrote in an article entitled "Calcium's Powerful Mysterious Ways" that, "Researchers are increasingly finding that the humble mineral calcium plays a major role in warding off major illnesses from high blood pressure to colon cancer" and that "You name the disease and calcium is beginning to have a place there" (David McCarron, a nephrologist at Oregon Health Sciences University).

Unfortunately, most doctors have not heard the news that their own journals, major newspapers and magazines are reporting that natural supplements, especially calcium, can cure and prevent disease.

The scientific evidence that calcium is the key to good and long health is overwhelming. Just 20 years ago, any doctor making the claim that calcium supplements could cure cancer would lose his license. Dr. Carl Reich lost his license for making this claim which the medical authorities of the day branded as "too simplistic". Yet today, the doctor's own Journals: The New England Journal of Medicine, The Journal of the American Medical Association, and the American Journal of Clinical Nutrition are all making the claim that calcium supplements can reverse cancer and that virtually no organ escapes calcium's influence. These journals have been quoted in our popular and respectable newspapers and magazines. We have come a long way, and still have a long way to go. At present, it is almost impossible to find a doctor who is aware of these scientific findings. Therefore, we must get the doctors to read their own Journals and then do an almost impossible task, get the American Medical Association and the Food and Drug Administration to do their jobs and endorse these scientific findings. When this finally occurs, over 90% of disease will be eradicated thereby eliminating massive pain and suffering, and we will be well on our way to curing America.

One does not have to be a rocket scientist to read simple articles in reputable newspapers, magazines quoting the doctor's own journals that are all saying that disease can be cured by diet. Also one can simply look at the millions of people around the world that never get sick and say, "Let's do what they do!" Unfortunately, all of their milk of the mountains is consumed as fast as it is produced. However, the Japanese could cure the world with their "milk of the oceans" known as coral calcium, the calcium factor of good health.

CHAPTER SEVENTEEN

QUESTIONS AND ANSWERS

The most frequent question asked the author is, "What do you do?" The response always begins with, "I have not taken a pill in over 30 years." Psychologically, taking pills is synonymous with taking drugs. Also, many people have difficulty swallowing pills. For most, many of the pills remain intact as they pass through the intestine undigested. The obvious solution is to do what

the author does. First, the author puts all of the non liquid nutrient pills and capsules into a blender to make a pulverized blend. He then uses a flour sifter to remove the broken up oversized capsule containers. The author takes 24 pills and capsules each day, and he has found that when pulverized, the blend fills a heaping teaspoon. Thus the author pulverizes a three month portion and puts it into a large bottle labeled "Hunza Powder", and then takes a heaping spoonful each day. Secondly, the nutrient blend should be taken at meal times, as for the elderly, this is the only time that they have sufficient acid in their stomachs to digest food. Thirdly, one glass of milk or one glass of apple juice should be taken with each meal so that the lactates or malates will keep the digested nutrients ionized even as they pass through the alkali duodenum, thereby allowing for greater absorption. Also, the consumption of fruits and vegetables with meals provides anions which enhance the absorption of nutrients.

The second most frequent question asked is, "which are the 24 pills that you take The answer is 3 coral calcium (1.5 grams), 2 vitamin-D (5000 IU each), 6 multivitamins (one-a-day), 6 multi-minerals (containing 60 trace minerals), 3 calcium (citrate), 1 magnesium citrate, 2 vitamin-C (60 mg each), 1 vitamin-E (500mg), and 10 milligrams cesium chloride. The result is Hunza Powder. The author takes a heaping teaspoon each day, usually mixed in a fruit slush or a banana shake.

The next most asked question is "What do I have to do to cure..... ?" The answer is that the body can cure itself of all disease if given the nutrients it needs. To begin with, the DNA which is the body's blueprint to cure itself and to stay young, only works "on a substrate of calcium". Thus the DNA will only repair the body when the body fluids are full of calcium and therefore alkaline. This is why many diseases are considered to be incurable, as without nutrition, the body remains acidic and DNA replication is inhibited.

So then, what are the nutrients that the body need to cure itself The answer begins with calcium. There is no such thing as a bad calcium nutrient. All calcium nutrients are good for producing a healthy body; however, some are better than others. For example, the consumption of coral calcium provides adequate calcium, magnesium and dozens of trace minerals for absorption by the body. Some calcium nutrients, such as calcium carbonate, are difficult for the body to absorb. This does not mean that they are not good, but rather that there are better choices. Also, there is no such thing as a bad coral calcium from Okinawa. They are all miracle minerals. However, some are better than others. The Japanese grade the coral based on magnesium content. The more magnesium a coral has, the higher it is graded. Consuming coral calcium can be classified in the same category as breathing as both fill the body with life sustaining oxygen. Most suppliers of coral calcium instruct you to take 2 to 3 capsules each day. But this is for maintaining good health. When you are sick, it is best to double-up to 4 to 6 per day. If you are really sick, with a disease such as cancer, Lupus, diabetes, etc., it is best to triple-up to 6 to 9 per day. The author has been told by many that a few months on the larger dose coral has successfully terminated their cancer, Lupus, Multiple Sclerosis and numerous other incurable diseases. Of course all of these people exposed themselves to sunshine and a host of other nutrients as well as the coral calcium.

Of course, other nutrients are also required, the most important being exposure to sunshine. Sun on the skin produces inositol triphosphate to regulate mineral disposition in the body and it also produces vitamin-D which allow the intestine to absorb large amounts of nutrients. The ultraviolet radiation from the sun striking the eyes stimulate the pituitary, pineal and hypothymus glands at the back of the eye to regulate the production of many hormones such as melatonin, serotonin and calcium-regulating calcitonin. Thus lack of sunshine on the body is responsible for a host of diseases, especially cancer. This sounds like a controversial statement, but not when you look at the facts. 'Me cancer-free black African is naked in the sun all day while the black American who avoids the sun like the plague, has three times the cancer rate of the sun worshipping white Americans. There is twice as much breast cancer in the Northern States as in the sunny Southern States. Prostate cancer goes up almost 300% from the sunny Mexican border to the Northern Canadian border. When exposure to the sun does trigger skin cancer, the victim is usually a white albino who already has five other mineral deficiency induced diseases, and is well on the way to developing the sixth.

Other important nutrient sources are multi-vitamins, which can be purchased inexpensively in all major stores. The instructions on the bottle may say to take one each day; however, the many cultures around the world that never get sick take about 100 times the amounts that is recommended in America. This means that you should take several every day, the author recommends at least 6 per day, as by the millions, these people have proven that there is no such thing as too much when it comes to vitamins and minerals. There is however, one exception, and that is large amounts of liquid calcium that can lead to hypercalcemia, if the body is not exposed to sunlight for at least one hour each day. Large quantities of coral calcium do not require sunshine as no amount of coral calcium can cause hypercalcemia. Also, trace minerals can be found in most health stores. Once again the instructions will say one per day, but 6 per day is recommended. Vitamin-D is also necessary to insure the absorption of nutrients. A minimum of 5000 IU is suggested. Extra boron, selenium, chromium, zinc, vitamin-A, vitamin-E and cesium is also recommended.

Although almost all degenerative diseases can be prevented and cured nutritionally if given enough time, people are always asking, "What can I do if I am terminal ?" A terminal cancer patient, for example, may be cured over a 6 month period by consuming the proper nutrients, but may only have 3 weeks to live. This situation requires a more potent nutrient treatment. A combination of common mineral salts can penetrate the tumor and then react to create concentrated and corrosive sulfuric acid which then kills the tumor. Also, cesium chloride, a

natural salt, and where it is found, cancer does not exist, can quickly alkalize and thereby terminate the cancer. Cesium is the most caustic mineral that exists, and when it enters the body, it seeks out all of the acidic cancer hotspots, dousing the fire of cancer, thereby terminating the cancer within days. Also, when dimethyl sulfoxide (DMSO) is rubbed near a painful cancer, the pain is removed and the DMSO causes the cesium to penetrate the cancer tumor much faster, thereby terminating the cancer much faster. DMSO is an approved drug in 125 countries around the world and 600 million people have used it therapeutically. Larger doses of vitamin-D will cause the body to alkalize faster bringing a speedy end to the cancer. Otto Warburg's oxygen respiration enzyme formula (Oxy-Plus, 520-684-4458) has also been proven to be effective against cancer.

Dr Karl Folker discovered CoQ IO in the 1960s while working for the giant pharmaceutical company Merck. He found it to eliminate cancer tumors in the breast, lung and stomach, Biochemical and Biophysical Research Communications, March 30, 1994. And finally, gold metal absorbed by the body has been found effective in recovering from cancer.

The following program has been found to be effective for cancer: 1. Consume 6 coral calcium capsules each day, 2 in morning, 2 in afternoon and 2 at night. 2. Consume 150 grams of mineral salts (5 per day) and then consume 100 grains of cesium chloride at 3 grams each day (one gram morning, noon and night, total 33 days). 3. Consume 100 milligrams of CoQ IO each day for 30 days. 4. Consume one Oxy-Plus (500 mg) three times each day. 5. Apply DMSO gel to skin nearest the cancer (or nearest to pain) twice a day. 6. Apply gold gel to skin nearest the cancer once each day. 7. Consume 6 vitamin-D tablets (5000 JU) each day, 2 in the morning, 2 in the afternoon and 2 at night. 8. Eat two bananas, and/or two large potatoes, two glasses of milk or two glasses of orange juice and eat raisins, tomatoes, spinach or broccoli every day (all contain lots of potassium, magnesium and calcium).

Expose your skin and face to a least two hours of sunshine every day with no skin block and no glasses (allows for the production of inositol triphosphate, calcitonin and vitamin D to help regulate crucial minerals such as calcium). Sun exposure is mandatory, even with s@ cancer.

Note:

1. All of the above ingredients are available at 520-684-4458. 2. This program will help to alkalize the body's fluids, resulting in the toxins, which are adhered to the cell surface, detaching themselves and entering the blood. The body will recognize the toxins as foreign invaders and respond by attacking them possibly causing flu-like symptoms like headaches, stomach aches and diarrhea. This is called "detoxing" and it means that the body is ridding itself of cancer inducing compounds.

After the cesium has been consumed (33 days) the cancer will be benign (only a biopsy can prove this). Continue taking all of the other nutrients except for the DMSO which should only be used for pain control.

The author has witnessed numerous people with terminal cancers who have employed the above program successfully. In the author's web site (www.cureamerica.net), and in the Testimonials section of this book, numerous testimonials are provided by prestigious Americans. The author has also witnessed hundreds of other less prestigious Americans cure their incurable diseases. Although their testimony is considered hearsay and unscientific, examining their medical records, which state that they are all terminal, and then matching them to the now healthy bodies, is very exciting. Pancreatic cancer for example is a death sentence. When a tearful Ray explained that his mother was only given less than 3 months to live due to a metastasized pancreatic cancer, he readily defied his doctors and put her on the cesium program. That was 3 years ago and his mother recently remarried and is currently on her second honeymoon. A young lady in Oklahoma with metastasized cancer was scheduled for a double mastectomy and colonoscopy prior to undertaking the cesium program. Today she is ecstatic as she has both breasts and her rectum is intact.

Alkalizing the body with nutrition allows the body to cure itself, even from previously incurable diseases. Nobel Prize winner, Otto Warburg complained in 1966 that because the agnostics were in control, millions of men and women would have to die needlessly from cancer. Today the agnostics are still in control, but their control has weakened substantially, due to information exchange by computers and the internet. Warburg was right as millions of Americans did die. The time is ripe to end the needless suffering, pain and death caused by curable degeneration diseases such as cancer and heart disease. The time has come to cure America.

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CANDIDA

Selenium deficiency and anemia appear to be the biggest factors in promoting candida growth. Years ago when I had hypoT I also had a severe candida infection. I found a book titled "Candida: Silver (Mercury) Fillings and the Immune System" which eventually led me to getting my mercury fillings removed. Following this and supplementation with zinc and selenium, my candida and hypoT both ended.

Experiments with animals show that candida growth can be increased by selenium deprivation and reduced by selenium supplementation. Since mercury depletes selenium, it makes sense that candida is higher when there are mercury fillings in the teeth.

Other studies show that anemia and iron deficiency increase candida growth. There are some studies suggesting that B12 and folic acid deficiencies may be involved in candida, since deficiencies of these lead to anemia. In anemia and iron deficiency friendly bacteria cannot grow well in the body. A lack of these bacteria probably is a key factor which promotes candida growth, since candida is a fungal growth rather than a bacteria growth.

Another study showed that women with recurrent vulvovaginal candidiasis are deficient in zinc compared to normals and that only a mild zinc deficiency is necessary for this recurring problem.

Basically it seems that the deficiencies associated with candidiasis correlate very well with the deficiencies associated with hypothyroidism. The key nutrient deficiencies are probably selenium, zinc, iron, B12, and folic acid.

Probably the best indicator of the level of candida growth in the body is the coating on the tongue. The more white coating there is, the more candida there probably is throughout the body. We want to get to the point where our tongues are clear, pink, and not sore.

The following study shows that candida albicans has a higher resistance to elevated concentrations of copper than baker's yeast. This may mean that in hypothyroidism, when zinc is low and copper is high, candida growth will not be suppressed by copper, which is normally toxic to fungal infections.

Proc Natl Acad Sci U S A 2000 Mar 28;97(7):3520-5

The high copper tolerance of Candida albicans is mediated by a P-type ATPase.

Weissman Z, Berdicevsky I, Cavari BZ, Kornitzer D

Department of Molecular Microbiology, The Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa 31096, Israel.

The pathogenic yeast *Candida albicans* has higher resistance than the baker's yeast *Saccharomyces cerevisiae* to elevated concentrations of copper. To understand the basis of this differential resistance, we performed a functional screen for *C. albicans* genes involved in copper detoxification. Here, we report the isolation of two such genes: a metallothionein, CaCUP1, and a copper-transporting P-type ATPase, CaCRP1. Both genes are induced by extracellular copper. Gene disruptions indicated that the copper extrusion pump is responsible for the unusual resistance of *C. albicans* to copper, whereas the metallothionein is responsible for the residual copper resistance of the CaCRP1Delta mutant. We show further that under acidic and anaerobic conditions, such as prevail in the natural niche of *C. albicans*, the digestive tract of animals, CaCRP1 function becomes essential for survival in the presence of even very low copper concentrations. These observations suggest that copper in the gastrointestinal tract may present a toxic challenge to which enteric organisms had to adapt.

The following studies show that selenium is a key nutrient in the control of candida albicans.

J Nutr 1986 May;116(5):816-22

The response of selenium-deficient mice to Candida albicans infection.

Boyne R, Arthur JR

The effects of selenium deficiency on the responses to *Candida albicans* infection were examined in mice. When selenium-deficient and selenium-supplemented mice were given i.v. injections of 0.1 ml suspensions of 1×10^5 or 5×10^4 *C. albicans* in 0.9% sterile saline, deaths in the selenium-deficient animals started after 2.5-3.5 d compared with 7-8.5 d in the selenium-supplemented animals. Further studies demonstrated that 3 d after an i.v. injection of 1×10^5 *C. albicans*, significantly more of the microorganisms were found in the kidneys (P less than 0.001), livers (P less than 0.025) and spleens (P less than 0.01) of the selenium-deficient mice compared with the same organs of selenium-supplemented animals. Selenium deficiency was also demonstrated to impair the ability of mouse neutrophils to kill *C. albicans* in in vitro tests. The possible

relationships of this defect in function to decreased resistance to *C. albicans* infection is discussed.

J Comp Pathol 1986 Jul;96(4):379-86

An in vivo and in vitro study of selenium deficiency and infection in rats.

Boyne R, Arthur JR, Wilson AB

Selenium deficiency in rats impairs the ability of neutrophils and peritoneal macrophages to kill *Candida albicans* organisms in vitro. In contrast, killing of *Salmonella typhimurium* and *Staphylococcus aureus* organisms is unaffected by the deficiency. Survival of rats after intraperitoneal injection of 8×10^7 *S. aureus* organisms was not affected by Se deficiency, but a 5-fold increase in the dose (4×10^8 *S. aureus* organisms) led to a significantly greater mortality in the Se deficient rats.

Indian J Biochem Biophys 1994 Oct;31(5):427-9

Effect of experimental selenium deficiency and its supplementation on the candidacidal activity of neutrophils in albino rats.

Kukreja R, Khan A

Department of Biochemistry, Nagpur University.

The role of selenium in the diet of rats has been examined with respect to the neutrophil functions. Feeding of Se-deficient diet for 75 days resulted in reduction in candidacidal activity, superoxide production, oxygen consumption, glucose utilisation and glutathione peroxidase activity. Supplementing the diet with Se for 30 days resulted in partial restoration of all the activities.

Biotin deficiency may also be involved in candida albicans.

Semin Dermatol 1991 Dec;10(4):296-302

Skin manifestations of biotin deficiency.

Mock DM

Department of Pediatrics, University of Iowa Hospitals and Clinics, Iowa City 52242.

This article reviews current knowledge concerning the dermatologic manifestations of biotin deficiency. Biotin is a water-soluble vitamin that acts as an essential cofactor for four carboxylases, each of which catalyzes an essential step in intermediary metabolism. For example, acetyl-CoA carboxylase catalyzes the rate-limiting step in fatty acid elongation. In infants, children, and adults, deficiency of biotin causes alopecia and a characteristic scaly, erythematous dermatitis distributed around body orifices. The rash closely resembles that of zinc deficiency. *Candida albicans* often can be cultured from the skin lesions. Biotinidase deficiency, an inborn error, causes biotin deficiency, probably as a consequence of unpaired intestinal absorption, cellular salvage, and renal reclamation of biotin; biotinidase deficiency causes dermatologic manifestations similar to biotin deficiency. There is evidence that impaired fatty acid metabolism secondary to reduced activities of the biotin-dependent carboxylases (especially acetyl-CoA carboxylase) plays an etiologic role in the dermatologic manifestations of biotin deficiency. *Candida* infections secondary to impaired immune function might also contribute to the dermatitis of biotin deficiency.

Am J Obstet Gynecol 1986 Nov;155(5):1082-5

Zinc status in women with recurrent vulvovaginal candidiasis.

Edman J, Sobel JD, Taylor ML

Zinc status has been shown to influence various cell-mediated immunologic mechanisms. These cell-mediated mechanisms are important in preventing mucocutaneous infections caused by *Candida albicans*. This study evaluated the relationship between zinc status and recurrent vaginal candidiasis by comparing plasma and erythrocyte zinc in 29 patients with recurrent vaginal candidiasis and 20 control subjects matched for age, race, and parity. The results indicated that there was a significantly lower level of plasma zinc in women with recurrent vaginal candidiasis (81 ± 11.6 mg/dl) than in the control subjects (91 ± 14.2 mg/dl) with a significant value of $p = 0.015$. These differences in plasma zinc levels were even greater when adjusted for dietary zinc and supplemental zinc with the use of analyses of covariance. No differences in erythrocyte zinc measurements were found between the two groups. These results suggest that mild zinc deficiency is associated with recurrent vaginal candidiasis and may play a role in the susceptibility of women to recurrent vaginal candidiasis.

The role of iron deficiency in experimentally-induced oral candidosis in the rat.

Rennie JS, Hutcheon AW, MacFarlane TW, MacDonald DG

In comparison with normal rats, those with iron deficiency anaemia showed no significant difference in susceptibility to experimental infection with *Candida albicans* although anaemic rats had a significantly greater incidence of persistent infection. These findings support the suggestion that patients with chronic candidosis should be investigated for iron deficiency.

Arch Oral Biol 1982;27(6):497-503

Experimental oral infection with the yeast *Candida albicans* in mice with or without inherited iron-deficiency anaemia (sla).

Sofaer JA, Holbrook WP, Southam JC

The role of iron deficiency in the development of oral candidosis was investigated using the mouse mutant sex-linked anaemia (sla). Susceptibility was assessed in terms of the recovery of organisms, particularly from oral swabs, and histological evidence of infection approximately 10 days after the last exposure to *Candida albicans*. The influence of three factors was studied in mixed groups of normal and anaemic mice: mode of inoculation, treatment with tetracycline and treatment with hydrocortisone. The most susceptible group had received drinking water containing tetracycline (1 mg/ml), hydrocortisone (0.1 mg/ml) and candida (5×10^4) c.f.u./ml for 6 days). Anaemic mice showed a rather higher rate of recovery of organisms and more frequent histological evidence of infection than normal mice in certain groups. Neither of these tendencies was statistically significant alone but, taken together, they suggest that some small difference of susceptibility may exist between normal mice and mice with sla. The mouse model could be of value in studying the influence of several other inherited disorders on susceptibility to candidosis.

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RAPE IN A DIFFERENT GUISE

<http://www.living-foods.com/board/read.php?f=1&i=21641&t=21641>

Dear Editors

Recently I bought a cooking oil that's new to our supermarkets, Canola Oil. I tried it because the label assured me it was lowest in "bad" fats. However, when I had used half the bottle, I concluded that the label told me surprisingly little else and I started to wonder: where does canola oil come from?

Olive oil comes from olives, peanut oil from peanuts, sunflower oil from sunflowers; but what is a canola? There was nothing on the label to enlighten me, which I thought odd. So, I did some investigating on the Internet. There are plenty of official Canola sites lauding this new "wonder" oil with all its low-fat health benefits. It takes a little longer to find sites that tell the less palatable details.

Here are just a few facts everyone should know before buying anything containing canola. Canola is not the name of a natural plant but a made-up word, from the words "Canada" and "oil". Canola is a genetically engineered plant developed in Canada from the Rapeseed Plant, which is part of the mustard family of plants.

According to AgriAlternatives, The Online Innovation, and Technology Magazine for Farmers, "By nature, these rapeseed oils, which have long been used to produce oils for industrial purposes, are... toxic to humans and other animals". (This, by the way, is one of the websites singing the praises of the new canola industry.)

Rapeseed oil is poisonous to living things and is an excellent insect repellent. I have been using it (in very diluted form, as per instructions) to kill the aphids on my roses for the last two years. It works very well; it suffocates them. Ask for it at your nursery. Rape is an oil that is used as a lubricant, fuel, soap and synthetic rubber base and as a illuminate for color pages in magazines.

It is an industrial oil. It is not a food. Rape oil, it seems, causes emphysema, respiratory distress, anemia, constipation, irritability, and blindness in animals and humans. Rape oil was widely used in animal feeds in England and Europe between 1986 and 1991, when it was thrown out. Remember the "Mad Cow disease" scare, when millions of cattle in the UK were slaughtered in case of infecting humans? Cattle were being fed on a mixture containing material from dead sheep, and sheep suffer from a disease called "scrapie".

It was thought this was how "Mad Cow" began and started to infiltrate the human chain. What is interesting is that when rape oil was removed from animal feed, 'scrapie' disappeared. We also haven't seen any further reports of "Mad Cow" since rape oil was removed from the feed. Perhaps not scientifically proven, but interesting all the same. US and Canadian farmers grow genetically engineered rapeseed and manufacturers use its oil (canola) in thousands of processed foods, with the blessings of Canadian and US government watchdog agencies. The canola supporting websites say that canola is safe to use. They admit it was developed from the rapeseed, but insist that through genetic engineering it is no longer rapeseed, but "canola" instead.

Except canola means "Canadian oil"; and the plant is still a rape plant, albeit genetically modified. The new name provides perfect cover for commercial interests wanting to make millions. Look at the ingredients list on labels. Apparently peanut oil is being replaced with rape oil. You'll find it in an alarming number of processed foods. There's more, but to conclude: rape oil was the source of the chemical warfare agent mustard gas, which was banned after blistering the lungs and skins of hundred of thousands of soldiers and civilians during W.W.I. Recent French reports indicate that it was again in use during the Gulf War.

Check products for ingredients. If the label says, "may contain the following" and lists canola oil, you know it contains canola oil because it is the cheapest oil and the Canadian government subsidizes it to industries involved in food processing.

I don't know what you'll be cooking with tonight, but I'll be using olive oil and old-fashioned butter, from a genetically unmodified cow.

Here is more information.....

Canola oil from the rape seed, referred to as the Canadian oil because Canada is mainly responsible for it being marketed in the USA. The Canadian government and industry paid our Federal Food and Drug Administration (FDA) \$50 million dollars to have canola oil placed on the (GRAS) List "Generally Recognized As Safe". Thus a new industry was created. Laws were enacted affecting international trade, commerce, and traditional diets. Studies with lab animals were disastrous. Rats developed fatty degeneration of heart, kidney, adrenals, and thyroid gland. When canola oil was withdrawn from their diets, the deposits dissolved but scar tissue remained on all vital organs. No studies on humans were made before money was spent to promote Canola oil in the USA.

Adrenoleukodystrophy (ALD) is a rare fatal degenerative disease caused by a build up of long-chain fatty acids (c22 to c28) which destroys the myelin (protective sheath) of the nerves. Canola oil is a very long chain fatty acid oil (c22). Those who will defend canola oil say that the Chinese and Indians have used it for centuries with no effect, however it was in an unrefined form.* (* taken from FATS THAT HEAL AND FATS THAT KILL by Udo Erasmus.)

My cholesterol level was 150. After a year using Canola oil I tested 260. I switched back to pure olive oil and it has taken 5 years to get it down to 160. Thus began this project to find answers since most Doctors will say that Canola oil is O.K.

My sister spilled Canola oil on a piece of fabric, after 5 pre-treatings and harsh washings, the oil spot still showed. She stopped using Canola oil, wondering what it did to our insides if it could not be removed from cloth easily.

Our Father bred birds, always checking labels to insure there was no rape seed in their food. He said, "The birds will eat it, but they do not live very long."

A friend, who worked for only 9 mo. as a quality control taster at an apple-chip factory where Canola oil was used exclusively for frying, developed numerous health problems. These included loose teeth & gum disease; numb hands and feet; swollen arms and legs upon rising in the morning; extreme joint pain especially in hands, cloudy vision, constipation with stools like black marbles, hearing loss; skin tears from being bumped; lack of energy; hair loss and heart pains. It has been five years since she has worked there and still has some joint pain, gum disease, and numbness.

A fellow worker, about 30 years old, who ate very little product, had a routine check up and found that his blood vessels were like those of an 80 year old man. Two employees fed the waste product to baby calves and their hair fell out. After removing the fried apple chips from the diet their hair grew back in.

My daughter and her girls were telling jokes. Stephanie hit her mom's arm with the back of a butter knife in a gesture, "Oh mom", not hard enough to hurt. My daughters arm split open like it was rotten. She called me to ask what could have caused it. I said, "I'll bet anything that you are using Canola oil". Sure enough, there was a big gallon jug in the pantry.

Rape seed oil is a penetrating oil, to be used in light industry, not for human consumption. It contains a toxic substance. (from encyclopedia). Even after the processing to reduce the erucic acid content, it is still a penetrating oil. We have found that it turns rancid very fast. Also it leaves a residual rancid odor on clothing.

Rape seed oil used for stir-frying in China found to emit cancer causing chemicals. (Rapeseed oil smoke causes lung cancer) Amal Kumar Maj.

The Wall Street Journal June 7, 1995 pB6 (W) pB6 (E) col 1(11 col in).
Compiled by Darleen Bradley.

Canola oil is a health hazard to use as a cooking oil or salad oil. It is not the healthy oil we thought it was. It is not fit for human consumption, do not eat canola oil, it can hurt you. Polyunsaturated or not, this is a bad oil.

Be Sure to also read this informative report written by leading health expert
Tom Valentine, Canola Oil Report.

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CELIAC DISEASE

Organ-Specific Autoantibodies Linked to Dietary Gluten in Celiac Disease Patients

WESTPORT, Sep 07 (Reuters Health) - Patients with celiac disease have high levels of diabetes- and thyroid-related autoantibodies that "disappear" when the patients are placed on a gluten-free diet.

The finding confirms the high prevalence of organ-specific autoantibodies in patients with celiac disease, and supports the theory that these antibodies are gluten-dependent, Dr. Alessandro Ventura, of the Universita di Trieste, Italy, and colleagues say in the August issue of the *Journal of Pediatrics*.

The investigators tested 90 children with celiac disease for serum antibodies to islet cells, glutamic acid decarboxylase, insulin, and thyroperoxidase. The overall prevalence of diabetes- and thyroid-related autoantibodies was 11.1% and 14.4%, respectively.

Prior studies have suggested that the presence of organ-specific autoantibodies in patients with celiac disease is "related to the presence of a second autoimmune disease." However, the fact that serum organ-specific autoantibodies tended to disappear in the current study when patients were placed on a gluten-free diet supports the position that these antibodies are at least partly gluten-dependent.

"A gluten-free diet started early may prevent the other autoimmune diseases frequently associated with celiac disease," Dr. Ventura and colleagues hypothesize. However, further studies will be needed to determine the clinical significance of the organ-specific autoantibodies in these patients and to confirm this hypothesis.

J Pediatr 2000;137:263-265.

Information from Mary Shomon:

CELIAC/AUTOIMMUNE THYROID DISEASE CONNECTION: A CURE FOR AUTOIMMUNE THYROID PROBLEMS?

The medical journal Digestive Diseases and Sciences has recently reported that a significant number of people who have autoimmune thyroid disease also have a condition known as celiac disease. Celiac disease causes the intestines to react abnormally to a substance called gluten. Gluten is a protein found in wheat, rye, barley, oats, spelt, kamut, and other related grains. Celiac disease is also sometimes called celiac sprue, sprue, or gluten intolerance. If you have celiac disease, your body may have difficulty absorbing nutrients from foods, leaving you malnourished, or deficient in key nutrients and vitamins. Celiac disease symptoms include various intestinal difficulties, recurring abdominal bloating and pain, nausea, gas, diarrhea, constipation, and other problems. The key news out of this research for thyroid patients is that researchers found that organ-specific autoantibodies (i.e., thyroid antibodies) can disappear after 3 to 6 months of a gluten-free diet. Don't rush right out and start on a gluten-free diet, however. You should have a blood test while eating your *regular* diet, and if you are positive, THEN go on the gluten-free diet to confirm the test results and diagnosis. For the percentage of people with autoimmune hypothyroidism who have celiac disease, diagnosis and a gluten-free diet may represent a permanent cure for their hypothyroidism. A detailed article, along with references and more information on celiac disease and the gluten-free diet, is located in an article at my website.

<http://thyroid.about.com/library/weekly/aa040700a.htm>

In persons with celiac disease, ingestion of gluten increases prolactin production.

Scand J Gastroenterol Suppl 1998;228:122-9

Coeliac disease: always something to discover.

Varkonyi A, Boda M, Endreffy E, Nemeth I, Timar E

Dept. of Paediatrics, Albert Szent-Gyorgyi Medical University, Szeged, Hungary.

The authors present more than 20 years' experience with coeliac disease, with a summary of their published studies. Hair shaft

characteristics were determined by scanning electron microscopy. Hair diameter was significantly lower and cuticular erosion scores higher in those who were not on gluten-free diets as compared to controls, showing a tendency towards normal values following start of gluten-free diets. Proton-induced X-ray emission showed significantly lower zinc content of the hair shaft in the group with acute coeliac disease and after a short-term diet, which approached the normal range only after a year-long diet. The serum prolactin levels in healthy controls and in coeliac patients on the diet were within normal limits, whereas in children with coeliac disease taking gluten in their meals, a significant hyperprolactinaemia was found. The erythrocyte glutathione content of coeliac children was elevated, and the glutathione disulfide level was significantly decreased, as compared to values in normal controls. The erythrocyte glutathione disulfide level and glutathione disulfide/erythrocyte glutathione ratio in coeliac children also differed from those in children with iron deficiency. With genotyping, the DQB1*0201/2 ($p < 0.00001$) and DR3 ($p < 0.00001$), DR7 ($p < 0.01$) alleles showed significant positive association with the disease.

CELIAC DISEASE AND VITAMIN D

From the Nutrition Almanac (4th Ed. pg. 83): "Celiac disease is indirectly related to a vitamin D deficiency resulting from structural damage and unabsorbed fats and calcium salts and vitamin D that are flushed out in the stool."

Organ-Specific Autoantibodies Linked to Dietary Gluten in Celiac Disease Patients

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CESIUM

Rough file:

"OBJECTIVES: We sought to determine which ion current predominantly affects defibrillation outcomes by using specific pharmacologic probes (lidocaine [a sodium channel blocking agent] and *cesium* [an outward potassium channel blocking agent]) in 26 swine. BACKGROUND: The effect of a drug on sodium or potassium channel conductance, or both, may affect defibrillation threshold values. However, it is unknown which ion channel predominates. METHODS: Each pig was randomly assigned to one of four treatment groups with two treatment phases: group 1 = placebo (D5W) in treatment phase I followed by placebo plus *cesium* in treatment phase II (n = 6); group 2 = lidocaine followed by lidocaine plus placebo (n = 7); group 3 = lidocaine followed by lidocaine plus *cesium* (n = 7); group 4 = placebo followed by placebo plus placebo (n = 6). Defibrillation threshold values and electrocardiographic measurements were obtained at baseline and at treatment phases I and II. RESULTS: Lidocaine increased defibrillation threshold values from baseline by 71% in group 2 (p = 0.02) and by 92% in group 3 (p < 0.01). There were no changes in defibrillation threshold values from baseline to D5W in groups 1 and 4. When D5W was added to lidocaine in group 2 and D5W in group 4, there were no significant changes in defibrillation threshold values. However, when *cesium* was added to lidocaine in group 3, the elevated defibrillation threshold values (mean +/- SD) returned to baseline values (from 15.7 +/- 3.46 to 7.55 +/- 3.19 J, p < 0.01). Cesium added to D5W in group 1 also significantly reduced defibrillation threshold values from 7.10 +/- 1.27 to 4.14 +/- 1.75 J (p < 0.01). The effect of *cesium* on defibrillation threshold values was similar between groups 1 and 3, regardless of lidocaine, such that these values were reduced by 40 +/- 14% and 51 +/- 18%, respectively (p = 0.28). CONCLUSIONS: *Cesium*, through potassium blockade, reverses lidocaine-induced elevation in defibrillation threshold values. The magnitude of defibrillation threshold reduction when *cesium* was added to lidocaine was similar to the defibrillation threshold reduction when *cesium* was added to placebo. Thus, inhibiting outward potassium conductance and prolonging repolarization decreases defibrillation threshold values independent of sodium channel blockade." [cesium.defibrillation.K and Na channel blockade.doc](#)

"Our primary novel finding concerning cesium is that relatively large concentrations of this ion are able to block a small, but statistically significant fraction of outward potassium current for potentials less than approximately 50 mV positive to reversal potential. This effect is relieved at more positive potentials. We have also found that external rubidium blocks outward current with a qualitatively similar voltage dependence. This effect is more readily apparent than the *cesium* blockade, occurring even for concentrations less than that of external potassium. Rubidium also has a blocking effect on inward current, which is relieved for potentials more than 20-40 mV negative to reversal, thereby allowing both potassium and rubidium ions to cross the membrane. We have described these results with a single-file diffusion model of ion permeation through potassium channels. The model analysis suggests that both rubidium and *cesium* ions exert their blocking effects at the innermost site of a two-site channel, and that rubidium competes with potassium ions for entry into the channel more effectively than does *cesium* under comparable conditions." [cesium and rubidium effects on potassium currents.doc](#)

Lithium, cesium: "Using inductively coupled plasma source mass spectrometry, we have studied the red cell element concentrations of alcoholic subjects with different periods of abstinence before testing. We found consistently elevated red cell caesium concentrations and also reduced red cell selenium concentrations. These may represent persistent abnormalities in oxidation/anti-oxidation mechanisms, and red cell caesium in particular may be a long-term marker of alcohol dependence. Erythrocyte *lithium*, cerium and boron concentrations were also reduced in the abstinent alcoholic groups." [cesium high.selenium low in rbc of alcoholics.doc](#)

"*Cesium* ions block potassium channels in biological membranes in a voltage dependent manner." [cesium blocks inward potassium current.doc](#)

The effects of cesium were tested by a researcher on himself: "There was an initial general feeling of well-being and heightened sense perception. A gradual decrease in appetite was noted initially before it was stabilized at a later date. Discontinuation of rich bread meals resulted in pre-nausea sensation which was followed by diarrhea 48 hr later. **The institution of high potassium nutrition decreased the feeling of nausea and abolished diarrhea.** A "tingling sensation in the lip and cheek regions was experienced 15 min subsequent the *cesium* chloride dosage compared to same sensation occurring at moderate intensity in hands and feet at end of the experiment. No adverse effects of CsCl were noted in performance of mathematical analyses or in driving skill. It is concluded that CsCl is devoid from toxicity provided adequate diet and supplements are administered." [cesium effects on a human.single case.doc](#)

"*Cesium* attenuates conditioned avoidance response in rats and mice."

"Two months after the nuclear accident of Chernobyl, postmortem measurement of radiocaesium (137 Cs and 134 Cs) were started in different organs to study incorporation, organ distribution, and kinetics. 250 corpses were examined between July 1986 to August 1987 in the Department of pathology, St. P"oltien. **Highest concentrations were found in skeletal muscles, with a median value of 2.3 pCi/g wet weight (80-90% of the total incorporated dose), followed by liver, lung, spleen, kidneys, thyroid gland, heart, blood and brain**, with values between 0.8 and 1.3 pCi/g. No caesium was detectable in fatty tissue. During the observation period an increase in caesium concentration was observed in almost all organs. The concentration almost doubled within 10 months in skeletal muscles. Only the lung demonstrated a decrease in the radiocaesium concentration within the first months, which can be explained only by inhalation of radiocaesium. **A statistically significantly higher caesium concentration in most organs was found in females as compared with males. A possible explanation is the known lower urinary caesium concentration in women. Statistically significant correlations were found between caesium concentration and nutritional status, presence of malignancy, and the most recent intravital serum creatinine value.**" [cesium.postmortem levels in Chernobyl victims.doc](#)

"The model analysis suggests that both rubidium and *cesium* ions exert their blocking effects at the innermost site of a two-site channel, and that rubidium competes with potassium ions for entry into the channel more effectively than does *cesium* under comparable conditions." [cesium and rubidium effects on potassium currents.doc](#)

"From the 137Cs/40K ratios it was found that *cesium* rather than potassium was selectively taken up from the soils by fungi such as *Suillus granulatus* and *Lactarius hatsudake*. [cesium and potassium in mushrooms.doc](#)

Cesium-137 was detected in most samples of dried and raw shiitake (*Lentinus edodes* (Berk.) Sing.). [cesium and](#)

The authors' result show that new types of dietary cellulose and composite food additives based on alfalfa polymers have rather pronounced antiradioactive properties against Cs-137 and Sr-85. This makes it necessary to organize the manufacture of these food additives whose daily dose of 12-20 should be supplemented into human diet every day. [cesium.alfalfa may block absorption.doc](#)

The levels of radiocesium in meat were reduced by a combination of countermeasures such as special feeding, use of **cesium** binders (bentonite and Prussian blue), [cesium is bound by bentonite.doc](#)

Practical experience gained after the Chernobyl accident has shown that both clay minerals and hexacyanoferrates are effective in preventing high radiocaesium levels in animal products. Chemicals such as bentonite clays and CaCO₃, [cesium binders.doc](#)

The depressive patients had reduced blood levels of caesium which increased towards normal on recovery. This finding is discussed in relation to pertinent neurochemical and behavioural effects of caesium. [cesium low in depression.doc](#)

These results indicate a specific neurosuppressant action of CsCl on mouse CNS and suggest exploration of this alkali earth metal for antipsychotic-like activity. [cesium.antidepressant antipsychotic effect.doc](#)

We explored the clearance of **cesium** in man and found that an oral dose of 50 mg maintains elevated blood **cesium** levels for 80 days. **Cesium** is accumulated mainly in the red blood cell fraction. Larger doses (6-9 grams) produce no observed harmful effects and maintain elevated blood levels of **cesium** for more than a year. [cesium clearance by braverman.doc](#)

The biological half-life of ¹³⁷Cs and its organ distribution were investigated in mice fed various potassium-deficient diets. The biological half-life, which was 6.1 days in mice receiving the normal level of potassium, became longer as the dietary potassium content decreased, and ¹³⁷Cs was hardly excreted from the body when dietary potassium content was restricted to 200 mg/kg or less. The muscle showed the highest concentration of ¹³⁷Cs in both mice that had sufficient amounts of potassium and those that were potassium-deficient. Clearance of ¹³⁷Cs from tissues was generally suppressed when mice were fed a potassium-deficient diet, but the relative distribution pattern of ¹³⁷Cs was not affected by dietary potassium content. These results suggest that dietary potassium intake, which may vary with eating habits, affects the biological half-life of ¹³⁷Cs in humans. [cesium half-life decreased by potassium intake.doc](#)

Cesium chloride administration causes ventricular tachyarrhythmias in dogs, with many of the features of the clinical long QT syndrome. [cesium-induced arrhythmias.doc](#)

Cesium-accumulating bacteria, strains CS98 and CS402, were isolated from soil by a radioactive autoradiographic method using ¹³⁷Cs. These strains displayed the rod-coccus growth cycle and contained mesodiaminopimelic acid, mycolic acids, and tuberculostearic acids. [cesium accumulating bacteria.doc](#)

Intracellular calcium plays an essential role in regulation of many cellular processes, but increases in internal calcium levels can also exacerbate pathophysiologic or pharmacologic responses, in particular myocardial arrhythmias. Pharmacologic increases in intracellular calcium may be obtained by opening calcium channels, either directly or indirectly, or by increasing calcium release from intracellular stores. In this study, **cesium** chloride administered intracoronarily (i.c.) through the left anterior descending coronary artery (LAD) dose-dependently elicited ventricular arrhythmias. Glyburide (3 micrograms/kg/min i.c.), clofilium (1 micrograms/kg/min i.c.) or ryanodine (0.03 micrograms/kg/min i.c.) exacerbated arrhythmias. [cesium induced arrhythmias and calcium.doc](#)

The chloride salts of lithium (Li⁺) and **cesium** (Cs⁺) were evaluated for their ability to influence the growth of Sarcoma I implants in A/J mice. The administration of daily doses of either 1 or 3 mEq/kg CsCl to these mice reduced the incidence and size of tumor implants. This effect was not apparent in animals receiving a smaller dose (0.5 mEq/kg) of the same drug. At the time of sacrifice the serum level of Cs⁺ in this latter group was approximately half that recorded in animals receiving the higher doses of CsCl. No effect on tumor incidence or rate of growth was observed in animals receiving different doses of LiCl. Because of the similarities that existed between **cesium** and potassium, it was postulated that the effect of **cesium** was due to alterations in the intracellular composition of the tumor cells. Also, the possible role of cytotoxic agents in potentiating the inhibitory effect of **cesium** on tumors was discussed. [cesium inhibits growth of Sarcoma I tumors.doc](#)

Rubidium and **cesium** chlorides accelerated cAMP synthesis in rat brain cortex membranes, while other alkali metal chlorides had no influence on the rate of this process. The effect was dose-dependent and yielded above 2-fold activation of adenylate cyclase. [cesium and Rb activate cAMP synthesis.doc](#)

Title

Cesium therapy in cancer patients.

Author

Sartori HE

Source

Pharmacol Biochem Behav, 21 Suppl 1():11-3 1984

Abstract

The effect of **cesium** therapy on various cancers is reported. A total of 50 patients were treated over a 3 year period with CsCl. The majority of the patients have been unresponsive to previous maximal modalities of cancer treatment and were considered terminal cases. The Cs-treatment consisted of CsCl in addition to some vitamins, minerals,

chelating agents and salts of selenium, potassium and magnesium. In addition, a special diet was also instituted. There was an impressive 50% recovery of various cancers, i.e., cancer of unknown primary, breast, colon, prostate, pancreas, lung, liver, lymphoma, ewing sarcoma of the pelvis and adeno-cancer of the gallbladder, by the Cs-therapy employed. There was a 26% and 24% death within the initial 2 weeks and 12 months of treatment, respectively. A consistent finding in these patients was the disappearance of pain within the initial 3 days of Cs-treatment. The small number of autopsies made showed the absence of cancer cells in most cases and the clinical impression indicates a remarkably successful outcome of treatment.

Females may absorb or need more cesium than males. In a study where dogs were given radioactive ^{137}Cs : "The middle-aged dogs died significantly earlier due to complications of hematological dyscrasia compared to the juvenile and young adult dogs, and the middle-aged females died significantly earlier than the middle-aged males. [cesium--effects of \$^{137}\text{Cs}\$ on age and sex in dogs.doc](#)

Maternal exposure to either alkali metal reduced brain and testis weights of the developing offspring mice compared to controls. This suggests a delayed toxic effect on the CNS and endocrine organs. Coadministration of both salts negated this effect. [cesium-lithium interaction in maternal mice.doc](#)

Cesium (up to 20 mM) had no effect on the late inward current or the mechanical activity, but decreased the early outward current by 80 +/- 12%. Manganese (25 mM), which blocks sodium-calcium exchange, abolished the late inward current and the mechanical activity. Manganese also reduced the early outward current by 27 +/- 10%. Manganese and **cesium** together blocked all the effects of sodium removal. We conclude that removal of extracellular sodium interrupts a **cesium**-sensitive "background current, that may be related to the time-dependent pacemaker current. If. Sodium removal also causes gradual activation of a nonspecific conductance, which can ultimately depolarize the cells, and which may be gated by cytoplasmic calcium. [cesium and manganese effects on sodium removal.doc](#)

Zinc-, copper-, cobalt, and nickel hexacyanoferrates(II), despite showing a high caesium sorption capacity in vitro, were less effective in rats and are not suited for in vivo application, also because they may produce toxic side effects. As a consequence, the orally administered colloidal-soluble iron(III) hexacyanoferrates(II) ($\text{NH}_4\text{Fe}[\text{Fe}(\text{CN})_6]$ and $\text{KFe}[\text{Fe}(\text{CN})_6]$) have to be considered as the most valuable countermeasure against radiocaesium absorption for humans and domestic animals in the case of a severe nuclear accident in the future.

Manganese oxide, a non-hexacyanoferrate(II) compound with known in vitro caesium binding capacity, showed no inhibitory effect on radiocaesium absorption in rats. [cesium binding by manganese and hexacyanoferrates.doc](#)

The effect of a mixture of calcium alginate, iron (III) ferrocyanide and potassium iodide added to rat diet on ^{85}Sr , ^{137}Cs and ^{131}I metabolism and health was investigated in female rats after four weeks of treatment. The retention of these radioisotopes was determined in the whole body and critical organs six days after ^{85}Sr and ^{137}Cs and one day after ^{131}I oral administration. The health effect of the mixture was evaluated by measuring body weights, haematological parameters, concentrations of iron, zinc and manganese in the kidneys, liver and femur, bone parameters (femur composition and morphometry) and by a histopathological examination. The mixture reduced ^{85}Sr retention in the femur 11 times, ^{137}Cs retention in the thigh muscle 102 times and ^{131}I retention in the thyroid 134 times. Treated animals were in good health and the only differences found between the control and experimental rats were slightly lower haemoglobin values in the blood and a slightly lower iron concentration in the liver. It is concluded that the mixture was very efficient for decreasing body retention of three important fission products and that it can be used over long periods without causing adverse health effects. [cesium retention factors.doc](#)

The author has treated 370 cases of skin cancer of the nose with **Cesium-137** brachytherapy. The excellent results with a low recurrence rate of 3% and good cosmetic results are compared with those reported on the literature. The method is more elegant than any reconstructive surgery, which should be reserved for extensive cases. [cesium and skin cancer of the nose.doc](#)

The experiments were carried out on 35 male (M) and female (F) rats contaminated by ingestion of **Cesium-- ^{137}Cs** for 38 or 84 days; the total Cs activity was 288 Bq 460 Bq, and respectively. The duration of forced swimming decreased significantly in the contaminated groups as compared with controls (n = 16). The active avoidance reaction in the shuttle-box shows an increase in F groups and a decrease in M groups. The total latency time of the same reaction was lower in F and M treated rats on the first day of learning. The score of aggressive behavior rose significantly, especially in group F. These results can be explained by the sex dependence of Cs accumulation and by the neurotoxic action of the radionuclide on several central neural areas including monoaminergic and endocrine mechanisms. [cesium--sex differences in accumulation.doc](#)

The effect of postnatal maternal ingestion of LiCl , CsCl or both during weaning period on the developing newborn was studied in the albino mouse. Maternal exposure to CsCl alone or in combination with LiCl reduced the weanling body weight from corresponding control which persisted for a subsequent 2 weeks after separation of the offspring from maternal breast feeding. This was compared to a moderate reduction in offspring growth by maternal Li-exposure during alkali metal-free period. Exposure of nursing dams to either alkali metals studied, but not their combination, decreased brain weight of the developing mouse. **The maternal Li-exposure caused a marked increase in female but not male offspring spleen weight as compared to a reduction of kidney weight from corresponding controls. Coadministration of CsCl with LiCl negated this sex-dependent Li-mediated changes of the offspring's tissue weights.** The maternal Li-treatment caused sex-dependent induction of offspring hepatic aldehyde dehydrogenase but not alcohol dehydrogenase. The results suggest that breast feeding by nursing dams ingesting these alkali metals could cause retarded growth during development. The Cs^+ appears to negate some of the changes produced by Li on brain and kidney weights. The interaction between Cs^+ and Li^+ may prove useful in minimizing some of the neonatal toxicity studied. [cesium and sex effects on lithium toxicity.doc](#)

Since cesium is found in muscles more than in other tissues, it seems logical that muscle building would use up more cesium. Also, males will have a higher reservoir of cesium than females because of their higher muscle mass. This may offer partial explanation why females are more subject to thyroid disease than males: "It was found that significantly higher contents of ^{137}Cs were present in the athletes. Furthermore, it was found that within the groups of athletes male subjects had significantly higher internal ^{137}Cs contamination per kilogram of body mass than the female subjects. An explanation for this is the different nutrition and the higher relative muscle mass of the athletes." [cesium incorporation higher in male athletes.doc](#)

Mass spectrographic and isotope studies have shown that potassium, rubidium, and especially **cesium** are most efficiently taken up by cancer cells. This uptake was enhanced by Vitamins A and C as well as salts of zinc and selenium. The quantity of **cesium** taken up was sufficient to raise the cell to the 8 pH range. Where cell mitosis ceases and the life of the cell is short. Tests on mice fed **cesium** and rubidium showed marked shrinkage in the tumor masses within 2 weeks. In addition, the mice showed none of the side effects of cancer. Tests have been carried out on over 30 humans. In each case the tumor masses disappeared. Also all pains and effects associated with cancer disappeared within 12 to 36 hr; the more chemotherapy and morphine the patient had taken, the longer the withdrawal period. Studies of the food intake in areas where the incidences of cancer are very low showed that it met the requirements for the high pH therapy. [cesium--high pH therapy for cancer.doc](#)

We studied the effects of permeant ions on the gating of the large conductance Ca^{2+} -activated K^+ channel from rat skeletal muscle. Rb^+ blockade of inward K^+ current caused an increase in the open probability as though Rb^+ occupancy of the pore interferes with channel closing. In support of this hypothesis, we directly measured the occupancy of the pore by the impermeant ion Cs^+ and found that it strongly correlates

with its effect on gating. This is consistent with the "foot-in-the-door model of gating, which states that channels cannot close with an ion in the pore. However, because Rb⁺ and Cs⁺ not only slow the closing rate (as predicted by the model), but also speed the opening rate, our results are more consistent with a modified version of the model in which the channel can indeed close while occupied, but the occupancy destabilizes the closed state. Increasing the occupancy of the pore by the addition of other permeant (K⁺ and Tl⁺) and impermeant (tetraethylammonium) ions did not affect the open probability. To account for this disparity, we used a two-site permeation model in which only one of the sites influenced gating. Occupancy of this "gating site interferes with channel closing and hastens opening. Ions that directly or indirectly increase the occupancy of this site will increase the open probability. [potassium channel gating and blocking by Ca, Rb, Cs.doc](#)

The mechanism by which magnesium therapy suppresses some ventricular tachyarrhythmias characterized by a prolonged QT interval (e.g., torsades de pointes) is unknown. Since early afterdepolarizations have been proposed as a cause of the long QT syndrome and the related ventricular tachyarrhythmias, we hypothesized that magnesium therapy would suppress both the early afterdepolarizations and the ventricular arrhythmias. The present study was performed to test that hypothesis. Using monophasic action potentials (MAP) recorded with a contact electrode from the right ventricular endocardium to demonstrate early afterdepolarizations, **cesium** chloride (168 mg/kg iv) was administered before, during, and 1 to 2 hr after discontinuation of a magnesium infusion (1 to 2 mg/kg/min for 20 to 30 min). Before magnesium infusion, **cesium** induced early afterdepolarizations that were 49.7 +/- 1.6% (mean +/- SE) of the amplitude of the corresponding monophasic action potential. The amplitude of the early afterdepolarization decreased to 31.2 +/- 3.8% of the MAP amplitude during magnesium infusion (p less than .003) and increased to 48.0 +/- 4.0% 1 to 2 hr after termination of the magnesium infusion (p less than .003). **Cesium** induced sustained monomorphic ventricular tachycardia, torsades de pointes, or ventricular fibrillation in 12 of 13 dogs before magnesium infusion, and in eight of 11 dogs 1 to 2 hr after stopping infusion, but in only three of 13 dogs during magnesium infusion. **Cesium** prolonged the corrected QT interval from 338 +/- 16 msec (control) to 387 +/- 14 msec before (p less than .003), 356 +/- 12 msec during (p less than .003), and 406 +/- 16 msec after stopping the magnesium infusion (p less than .003).(ABSTRACT TRUNCATED AT 250 WORDS) [cesium induced tachyarrhythmias stopped by magnesium.doc](#)

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CHOCOLATE

Chocolate is high in copper but for some reason it does not seem to be a good food for hypers which the high copper content would suggest. Because of this and other reasons, I developed a suspicion that chocolate is high in cadmium. Searching for medical studies on cadmium and chocolate led me to only two studies. The first study below is very suggestive that my suspicion is correct and that cocoa beans may be high in both cadmium and lead. The second study confirms that chocolate is high in cadmium (and also nickel). It's possible that the cadmium is introduced to the cocoa during processing, possibly by contact with galvanized containers, and is not natural to the food.

Nahrung 1987;31(5-6):635-6

Lead and cadmium content in cocoa beans (short communication).

Prugarova A, Kovac M

Food Research Institute, Bratislava, Czechoslovakia.

The choice of cocoa beans as the experimental and sample material for study of the contamination with lead and cadmium was inspired by high Pb and Cd limits in foods made on its basis (cocoa powder, chocolate) as well as by the relatively high proportion of these foods in human nutrition. For Cd, the limits in food products are within the range of 0.01 mg X kg⁻¹ (milk) to 1.0 mg X kg⁻¹ (kidneys) whereas the limits for lead range between 0.1 mg X kg⁻¹ (e.g. milk) and 10.0 mg X kg⁻¹ (e.g. tea, yeast, crustaceans, molluscs). Limits for Pb and Cd in foods made on cocoa bean basis are given in Table 1.

Food Addit Contam 1994 May-Jun;11(3):351-63

Beverages as a source of toxic trace element intake.

Pedersen GA, Mortensen GK, Larsen EH

National Food Agency of Denmark, Central Laboratory, Soborg.

Beverages of different kinds have been investigated for their content of lead, cadmium, nickel, chromium, arsenic and mercury. About a ten times higher lead concentration was found in wine than in most other beverages. **Cocoa was high in cadmium and nickel and some vegetable juices contained high levels of nickel.** The daily intake of trace elements from beverages was estimated. Wine was still the most significant source of lead even if the bottles did not have lead capsules. By consumption of half a bottle per day the daily intake of lead would be doubled and it would contribute 12% of Provisional Tolerable Weekly Intake. **Cocoa is an important source of cadmium and nickel,** and consumption of tea as well as vegetable juices could increase the nickel intake significantly. The data are compared to Danish maximum limits on lead and cadmium.

Title: Chocolate craving and liking.

Author(s): Rozin P Levine E Stoess C

Journal: *Appetite*. 1991 Dec; 17(3): 199-212 1991 0195-6663

Abstract: Liking and craving for chocolate and related substances were surveyed in a sample of University of Pennsylvania undergraduates (n = 249) and their parents (n = 319). Chocolate was highly liked in all groups, with a stronger liking by females. **Chocolate is the most craved food among females,** and is craved by almost half of the female sample (in both age groups). Although this craving is related to a sweet craving, it cannot be accounted for as a craving for sweets. **About half of the female cravers show a very well defined craving peak for chocolate in the perimenstrual period, beginning from a few days before the onset of menses and extending into the first few days of menses.** There is not a significant relation in chocolate craving or liking between parents and their children. The current motivation for chocolate preference seems to be primarily, if not entirely, sensory. Liking for chocolate correlates significantly with liking for sweets and white chocolate. The liking for the sensory properties could originate in innate or acquired liking based on the sweetness, texture and aroma of chocolate, or it could be based in part on interactions between the postingestional effects of chocolate and a person's state (e.g., mood, hormone levels). Based on correlational data, we find little evidence for a relation between addiction to chocolate or the pharmacological (e.g., xanthine-based) effects of chocolate and the liking for chocolate.

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COBALT

Rough file:

Cobalt is a relatively rare magnetic element with properties similar to iron and nickel. The two valance states are cobaltous (II) and cobaltic (III) and the former is the most common valance used in the chemical industry. Cobalt occurs in nature primarily as arsenides, oxides, and sulfides. Most of the production of cobalt involves the metallic form used in the formation of cobalt superalloys. The term "hard metal" refers to compounds containing *tungsten* carbide (80-95%) combined with matrices formed from cobalt (5-20%) and nickel (0-5%). For the general population, the diet is the main source of exposure to cobalt. In the occupational setting, exposure to cobalt alone occurs primarily during the production of cobalt powders. In other industrial exposures (e.g., hard metal, diamond polishing), additional agents (*tungsten*) modulate the toxicity of cobalt. Cobalt is an essential element necessary for the formation of vitamin B12 (hydroxocobalamin); however, excessive administration of this trace element produces goiter and reduced thyroid activity. In 1966, the syndrome "beer drinker's cardiomyopathy" appeared in Quebec City, Canada, and was characterized by pericardial effusion, elevated hemoglobin concentrations, and congestive heart failure. An interstitial pulmonary fibrosis has been associated with industrial exposure to hard metal dust (*tungsten* and cobalt), but not to cobalt alone. Exposure to cobalt alone produces an allergic contact dermatitis and occupational asthma. Treatment of cobalt toxicity is primarily supportive. [cobalt--high amounts can cause goiter and hypoT.doc](#)

This paper provides a short overview of cobalt-related diseases with particular reference to the potential carcinogenicity of cobalt compounds, and a review of a 10-year surveillance programme on plate painters exposed to cobalt in two Danish porcelain factories. Clinical experience and epidemiological studies have demonstrated that cobalt exposure may lead to severely impaired lung function, i.e. hard metal lung disease and occupational cobalt-related asthma, contact dermatitis and cardiovascular effects. However, the evidence for the carcinogenicity of cobalt and cobalt compounds is considered inadequate (IARC, 1991). Most frequently, exposure to cobalt occurs simultaneously with exposure to other elements known to pose a health risk, (e.g. nickel, arsenic, chromium, *tungsten*). The importance of cobalt as sole causal agent in hard metal lung diseases, cardiomyopathy and cancer are still a matter of controversy. In the two Danish porcelain factories, cobalt blue underglaze dyes have been used since 1888. In contrast to the exposure experience of hard metal factories, the exposure of plate painters occurs with only low trace levels of other potentially harmful compounds such as the carcinogenic metals nickel, arsenic and chromium. Consequently, the nearly-pure cobalt exposure makes the plate painters an attractive group for studies on the health effects of cobalt. During the period 1982-1992 the surveillance programme showed a profound reduction in the urine level of cobalt (Co-U) from 100-fold to 10-fold above the median level of the unexposed control subjects. In the same period, the airborne cobalt exposure declined from 1356 nmol/m³ to 454 nmol/m³, the Danish occupational exposure limit being 845 nmol/m³. In 1982, when the cobalt exposure was above the occupational exposure limit, the plate painters showed a chronic impaired lung function. The obstructive effects may be similar to some of the effects observed in hard metal workers. In 1988, a study on the effect of cobalt exposure at low levels revealed no inhibitory effects on thyroid function, but the ratio between T4 and T3 increased, indicating that low cobalt exposure may have an impact on the metabolism of thyroid hormones. Parallel studies were conducted on the metabolism and excretion of cobalt. The gastrointestinal uptake of soluble CoCl was considerably higher than the uptake of insoluble cobalt(II) oxide. In addition, it was demonstrated that ingestion of controlled amounts of the soluble cobalt compound resulted in significantly higher concentrations of cobalt in urine and blood (Co-B) from females compared with males (P < 0.01). Future studies will involve epidemiology and genotoxicity to evaluate the previous and present cancer risk, and detailed process-related exposure assessment studies to select the methods most reliable for surveillance of low-dose cobalt exposure. [cobalt--danish pottery worker study.sex differences.doc](#)

This study was conducted to investigate the physiological consequences of long-term moderate cobalt deficiency in beef cattle, which have not hitherto been studied in detail. Cobalt deficiency was induced in cattle by feeding two groups of animals either a basal corn silage-based diet that was moderately low in cobalt (83 micrograms Co/kg), or the same diet supplemented with cobalt to a total of 200 micrograms per kg, for 43 weeks. Cobalt deficiency was induced, as judged by inappetance, diminished growth gain and a markedly reduced vitamin B12 status in serum and liver. The long-term cobalt deprivation which was primarily a combination of reduced feed intake and a tissue vitamin B12 deficiency did not show evidence of a significant dysfunction of energy metabolism. The activities of glucose-6-phosphate dehydrogenase and cytochrome oxidase in liver remained unaffected by cobalt deficiency, nor was there a significant change in serum glucose level of cattle on the cobalt-deprived diet. **However, analysis of thyroid hormone status indicated a slight reduction of type I thyroxine monodeiodinase activity in liver accompanied by a significant reduction of the triiodothyronine level in serum.** The diminished liver vitamin B12 level resulted in significantly reduced folate level in this tissue, reduced concentrations of heme-depending blood parameters. Moreover cobalt deficiency or rather vitamin B12 deficiency was accompanied by a dramatic accumulation of the trace elements iron and nickel in liver. These results indicate that long-term moderate cobalt deficiency may induce a number of physiological changes in cattle, but a follow-up study, which excluded different feed levels by including a pair-fed control group, will be necessary to actually obtain the single effect of cobalt deficiency in cattle. [cobalt deficiency effects.doc](#)

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COPPER

COPPER CONTENT IN FOOD - (Milligrams)

1 oz baking chocolate (unsweetened, dark) - .748
1 Tbsp molasses, blackstrap - .284
1 cup whole milk - .50
1 avocado - .527
10 dried figs - .585
1 cup raisins - .498
1/4 lb beef liver - 3.2
1/4 lb lamb liver - 6.2
1/4 lb veal liver - 9.0
1 duck liver - 2.62
1 goose liver - 7.07
1 turkey liver - .512

NUTS -

1/2 Cup almonds - .59
1/2 C Brazil nuts - 1.07
1/2 C cashews - 1.41
1/2 C hazelnuts - .86
1/2 C peanuts - .31
1/2 C pecans - .57
1/2 C shelled pistachios - .76
1/2 C pine nuts - 1.16
1/2 C pumpkin or squash seeds - .95
1/2 C sesame seeds - 1.2
1/2 C sunflower seeds - 1.29
1/2 C walnuts - .70
2 Tbsp tahini (sesame seed butter) - .48

FISH -

1/4 lb cod - .57
1/4 lb haddock - .26
1/4 lb herring - .34
1/4 lb salmon - .22
1/4 lb trout - .37
1/2 cup tuna - .10

SHELLFISH -

1/4 lb crab - 1.47
1/4 lb lobster - 2.49
1/4 lb oysters - 1.36
1/4 lb scallops - .14
1/4 lb shrimp - .49
3.5 oz snails - .40
1 c asparagus - .20
1 c collard greens - .484
1 c cooked kidney beans .647
1 c cooked lentils - .54
1 c cooked lima beans - .519
1 c okra - .94
1 c parley - .293
1 c green peas - .257
1 c cooked split peas - .50
3 medium pimientos - .60
1 c potato - .388
1 lg baking potato - flesh and skin - .26
1 c pumpkin - .33
1 c soybean sprouts - .30
1 cup spinach - .32
1 sweet potato - .22
1 cup tomato juice - .246
1 cup yams - .484

Best Wishes,Chris

Copper and Hyperthyroidism

Thyroid and immune system health are crucially dependent upon copper. As far as I can see now, copper deficiency is the most important factor in the development of hyperthyroidism. Virtually all hyperts in the hyperthyroidism group have found that copper supplementation reduced their symptoms, usually within hours or a few days at most. Most have reported that within three to six months of beginning copper supplementation, they have been able to significantly reduce their intake of antithyroid drugs.

While copper is the big story in hyperthyroidism, it is not the whole story. If it were, it would have been discovered years ago. Proper copper metabolism interrelates with and depends upon many other nutrients.

Copper, Zinc, and Sex

One unique thing about copper is that women need more of it than men. This seems to be primarily because copper is required for the production of the enzymes which convert progesterone into estrogen. Men, however, require more zinc, which seems to be the mineral necessary to form the enzymes which convert progesterone into testosterone.

Studies show that copper intake in America is borderline or inadequate. Foods that contain copper, such as nuts and seeds, beans and other legumes, lobster, and crab, are not eaten, especially by women who need more copper, because of beliefs that these foods are fattening or contain toxic substances (shellfish). Other foods like beer and chocolate are good sources of copper but because of the other ingredients, alcohol in beer, and caffeine and sugar in chocolate, they are not consumed in amounts sufficient for women.

Because copper content of the average diet is marginal, men are generally able to get enough copper for two reasons: first, their requirement for copper is slightly less; second, most men drink beer. Beer contains reasonably high levels of two critical minerals: copper and selenium. Probably men have a drive to drink beer for its selenium content which is necessary for testosterone production, and as a by-product consume a lot of copper. Because copper slows down the thyroid, this is the probable reason that drinkers of beer put on weight and get a "beer-belly."

Women, on the other hand, driven by a desire to stay thin, generally avoid the high copper foods because of the perception (which is correct) that the high copper foods can cause weight gain.

Tobacco smoking

Other women start smoking tobacco for a similar reason: because of the perception that smoking makes you stay thin. I believe that there is truth to this perception, because it appears that the cadmium in tobacco smoke is a copper antagonist. This results in low copper levels, and when combined with a high-zinc, meat-based diet, results in higher thyroid output, a higher rate of metabolism, and staying thinner.

Unfortunately, for women there seems to be an interaction between estrogen and cadmium which results in high cadmium levels which not only depress copper, but depress zinc. Once zinc is depressed, the metabolic rate decreases and obesity sets in. Depending upon dietary intake of copper and zinc, cadmium can either push the woman to hypothyroidism (low zinc) or hyperthyroidism (low copper). The combination of [estrogen](#) and [cadmium](#) acts as an accelerator which pushes women one way or the other and makes the happy medium difficult to accomplish.

Copper and vitamins

I believe that many people probably consume a nutritionally adequate amount of copper in their diets. However, because copper absorption and utilization depend upon the presence of many other nutrients including many of the B complex vitamins, many people do not get an adequate amount of copper into their cells.

Many of the B Complex vitamins are essential for copper utilization and deficiencies of these vitamins are similar to copper deficiencies. Vitamins B-1 (thiamine), B-2 (riboflavin), B-3 (niacin), B-5 (pantothenic acid), biotin, and PABA all seem to work with copper and information about these can be found in separate pages on them.

Of all these B vitamins, I believe that biotin and PABA are the most important because they are usually the most neglected and probably under-represented in most B Complex and multiple vitamin supplements. Books on vitamins typically describe biotin as a vitamin which doesn't get deficient unless raw eggs are eaten and rarely even mention PABA as a possible deficiency. There are some sources which indicate that PABA is beneficial in hyperthyroidism which adds support to my belief that PABA is an important nutrient to assist copper metabolism. Often it seems that deficiencies of other nutrients, which are needed for copper metabolism, are the problem in hyperthyroidism. However, even when these other nutrients are inadequate, increasing copper intake seems to help.

The other side of the situation is that excessive amounts of the vitamins which facilitate copper metabolism may deplete copper further if copper is deficient. Vitamin C is essential for copper metabolism, but excess vitamin C, such as 5000-10000 mgs per day seems to deplete copper. It's important to have all the nutrients balanced and not to take an excessive amount of any one nutrient.

How does copper work in the body and what are the documented effects of copper deficiency in humans?

Copper is essential for maintaining the strength of the skin, blood vessels, and epithelial and connective tissue throughout the body. Deficiencies of copper can result in hernias, aneurysms, and blood vessel breakage manifesting as bruising or nosebleeds. If copper is important in cellular membrane structure, then a copper deficiency could seriously alter the movement of nutrients through cell walls.

Copper and Autoimmune Disease

Grave's disease is characterized as an autoimmune disease. This means that the immune system is not operating properly. Immune bodies known as immunoglobulins (IGs) are stimulating the thyrotropin receptors in the thyroid gland and this stimulation causes the thyroid to increase hormone output.

I think that it's obvious that healthy immune system function, like any biological function, is dependent upon an adequate supply of essential nutrients. It is not a great leap of faith to see that a deficiency of an essential nutrient could cause the immune system to malfunction.

There is very little scientific evidence that copper is involved in immune system function, but it is my belief that copper deficiency is the principal nutritional deficiency involved in autoimmune diseases. Approximately 80% of the people who suffer from autoimmune diseases are women. The most important nutrient that women need more of than men is copper. Any nutritional detective who is trying to find the culprit in autoimmune diseases should first suspect copper. Women need more copper and get autoimmune diseases more frequently. Men need less copper and generally don't get autoimmune disease. Copper deficiency is the obvious suspect.

What's the evidence? First of all, the main copper antagonist, zinc, is known to be involved in immune system function. Zinc and zinc containing herbs like ginseng are listed in many health books as immune system boosters. I believe that many health practitioners and autoimmune disease sufferers alike interpret this information incorrectly. They are recommending and using zinc supplements for the treatment of autoimmune dysfunction. I believe that this is completely incorrect and the last thing you would want to do in the case of an autoimmune disease is to stimulate the immune system by supplementing zinc.

Autoimmune diseases are characterized by an out-of-control immune system. To use a car analogy, the immune system, which is the system to maintain the proper functioning of the auto, could be represented by the mechanic. In the case of autoimmune diseases, the mechanic is out-of-control and ruining things rather than fixing them. Supplementing with zinc and stimulating the immune system would be like giving coffee to the out-of-control mechanic so that he works twice as fast and destroys twice as many things in the car.

If the immune system were under performing, then zinc would be a proper supplement to increase its functioning. But when the immune system is so overactive that it is causing damage to the body, then it's completely inappropriate. The proper nutrient to supplement would be zinc's antagonist, copper. Copper will decrease the stimulation to the immune system that zinc causes and enable the immune system function to slow down and perform normally.

Is there any evidence that copper is involved in the functioning of the immune system? Yes. There is a disease called Wilson's disease, which is characterized by the body's inability to properly metabolize copper and the copper accumulates in the liver, brain, and other organs to the point where it causes damage. One of the main medical treatments of Wilson's disease is the use of D-penicillamine, which is a drug which chelates (or grabs) metals, especially copper, and removes them from the body. Many Wilson's patients who are treated with penicillamine develop autoimmune diseases like lupus. Penicillamine chelates both copper and zinc and many patients also need to supplement zinc and B-6 (the B vitamin that helps zinc metabolism) to stay healthy. Penicillamine has also been shown to induce autoimmune disease in rats (study).

Another study shows that copper deficiency in mice impairs immune system function. "Dietary copper (Cu) was restricted in Swiss albino mice during five discrete intervals over a 9-wk period of perinatal development: gestation only (G), lactation only (L), 3 wk postlactation (PL), 1 wk after birth through postlactation (2/3L + PL), and lactation plus postlactation (L + PL). Biochemical and immunological status of mice in copper-deficient (-Cu) treatment groups in models G and L did not differ from that of copper-adequate (+Cu) controls. Signs of severe copper deficiency, such as low liver copper levels, and significant reductions in activity of plasma ceruloplasmin and splenocyte Cu-Zn superoxide dismutase were most evident in 6-wk-old mice from two groups, -Cu 2/3L + PL and -Cu L + PL. Mice in these groups were anemic and had small thymuses and enlarged spleens compared to controls receiving +Cu treatment. The -Cu mice demonstrated impaired antibody (plaque-forming cells, PFC) response to sheep erythrocytes, and the attenuation was proportional to copper deficiency, as judged by liver copper levels. Total plasma IgM levels were not greatly altered by -Cu treatment except in model L + PL. Total IgG levels were markedly reduced in this group and in the -Cu 2/3L + PL group. The PFC response of mice in the -Cu PL group was normal even though signs of copper deficiency were evident; however, the PFC response was reduced when -Cu treatment was extended to 5 wk and was reversible by switching to +Cu treatment. Splenocyte reactivity to B- and T-cell mitogens was not greatly different between groups. Incorporation of thymidine into DNA in the absence of mitogen was higher in -Cu mice. It is evident that severity of copper deficiency is related to degree of impaired immunity. Furthermore, severity of copper deficiency is dependent on duration and time of initiation of dietary copper restriction." (Copper deficiency during prenatal development: effects on the immune response of mice.)

In an experiment on calves, "in vitro Cu supplementation decreased ($P < .01$) lymphocyte blastogenic response."

One form of hypothyroidism is called Hashimoto's Disease. This is a form of hypothyroidism characterized by immune system dysfunction and is the hypothyroid version of Grave's Disease. Some people in the health field consider Grave's and Hashimoto's the same disease. While the actual thyroid function is different in the two diseases, one high and the other low, other characteristics of the diseases are very similar. For example in both diseases, patients might have thyroid eye disease (TED, ophthalmopathy, orbitopathy) or pretibial myxedema (swelling of the tissue at the front of the shin).

At this point in my research it looks like TED and pretibial myxedema are more the result of zinc deficiency than copper deficiency, but taking zinc without copper does not seem to be a wise decision in light of the fact that Hashimoto's and Grave's are both autoimmune diseases. Copper is necessary for the control of the immune system dysfunction, before zinc can be supplemented to control the fibroblast growth which is seen in TED and myxedema.

Copper and Hypothyroidism

Is copper deficiency involved in hypothyroidism? In one study it was found that copper deficiency enhances the effects of PTU-induced hypothyroidism. "Thus, copper-deficient and hypothyroid states were considerably enhanced when the 2 existed concurrently, giving added meaning and necessity to close surveillance of trace mineral concentrations and thyroid gland status."

Title

Interrelationships between athyroidic and *copper*-deficient states in rats.

Author

Oliver JW

Source

Am J Vet Res, 36(11):1649-53 1975 Nov

Abstract

Possible interrelationships of *copper*-deficient (*copper*-deficient ration) and hypothyroid (thiouracil treatment) states in rats were examined. Clinical signs, necropsy changes, and thyroxine concentrations were determined in 6 groups of rats treated as follows: group A--nontreated control; group B--thiouracil treated; group C--fed *copper*-deficient ration; group D--thiouracil treated and fed *copper*-deficient ration; group E--thyroid-stimulating hormone (TSH) treated; and group F--TSH treated and fed *copper*-deficient ration. Clinical signs occurred first and were most severe in the thiouracil-treated rats fed *copper*-deficient ration and included conformational changes and slower maturation, weakening of ear cartilage, middle ear changes (reflected by tilting of heads), and alopecia. Fatty infiltration of hepatic tissue was found in all rats fed *copper*-deficient rations, and considerable fluid retention occurred in rats fed *copper*-deficient ration and subjected to daily TSH treatment. Adrenal gland weights were 81% of control values (adjusted for body weight) in thiouracil-treated rats fed *copper*-deficient ration, and hypophysis weights were 114 and 154% of control values in thiouracil-treated rats and thiouracil-treated rats fed *copper*-deficient ration, respectively. Thyroid gland weights were 281% of control values in both thiouracil-treated rats and thiouracil-treated rats fed *copper*-deficient ration. Plasma thyroxine concentrations were markedly reduced (9% of control value) in thiouracil-treated rats fed *copper*-deficient ration. Thus, *copper*-deficient and hypothyroid states were considerably enhanced when the 2 existed concurrently, giving added meaning and necessity to close surveillance of trace mineral concentrations and thyroid gland status.

Some women with hypothyroidism also have galactorrhea, which is a condition of excessive production of prolactin, the hormone which causes breast milk secretion. The result is spontaneous release of breast milk and body weight gain which is the apparent result of the body being in a pregnancy-like state due to hormonal imbalance. There is a study suggesting that copper may be involved in the production of prolactin. There is a case of a woman who developed galactorrhea from a copper IUD. This association of galactorrhea with hypothyroidism could be evidence of a disturbance of copper metabolism in hypothyroidism.

Title

Normoprolactinemic galactorrhea in a fertile woman with a *copper* intra-uterine device (*copper* IUD).

Author

Giampietro O; Ramacciotti C; Moggi G

Source

Acta Obstet Gynecol Scand, 63(1):23-5 1984

Abstract

We report a case of galactorrhea in a normoprolactinemic fertile woman (30 years old) wearing a *copper* intra-uterine device (Gravigard). The Gravigard was first inserted in July 1977. In February 1979 our patient noted spontaneous galactorrhea, mainly on the left, but it was also present on the right, after breast pressure. X-ray film of the sella turcica, visual-field examination, thyroid function and basal prolactin levels were all within normal limits. In May 1979 the Gravigard was withdrawn and milk loss stopped finally in December 1979. In March 1980 the IUD was replaced; after only 3 days, mild spontaneous lactation again ensued, on the right side. The patient never took drugs which might have occasioned a prolactin rise. Possible explanations for this unusual phenomenon are discussed.

In a study on rats there is evidence that copper is necessary for proper iodine metabolism and consequently of proper thyroid hormone synthesis.

Title [The effect of *copper* on the metabolism of iodine, carbohydrates and proteins in rats]

Author

Esipenko BE; Marsakova NV

Source

Fiziol Zh, 36(2):35-43 1990 Mar-Apr

Abstract

Experiments on 156 rats maintained at ration with *copper* deficiency have demonstrated a decrease in the values of iodine metabolism in organs and tissues excluding the liver where a sharp increase in the concentration and content of inorganic iodine was observed. A disturbance

in indices of carbohydrate and proteins metabolism in the organism of animals is marked. A direct relationship with a correlation coefficient equaling 0.87-1.00 is determined between changes in the concentration of protein-bound iodine in blood and concentration of glycogen in the liver, skeletal muscles, albumins, alpha 1-, alpha 2-globulins, urea concentration; an inverse relationship with glucose, activity of blood lipo-dehydrogenase and liver mitochondria, aldolase, concentration of pyruvic and lactic acids is established as well. It is concluded that *copper* deficiency can exert both a direct effect on metabolic processes (as data from literature testify) and an indirect one disturbing iodine metabolism, i. e. sharply decreasing protein-bound iodine production by the thyroid gland.

COPPER

Copper is essential for maintaining the strength of the skin, blood vessels, and epithelial and connective tissue throughout the body. Deficiencies of copper can result in hernias, aneurysms, and blood vessel breakage manifesting as bruising or nosebleeds. If copper is important in cellular membrane structure, then a copper deficiency could seriously alter the movement of nutrients through cell walls. JJ

The following are metals which cause pulmonary fibrosis and therefore may be involved in working with copper in the production of collagen. These elements might be involved in thyroid function, along with tungsten (which combined with cobalt produces hard metal).

Schweiz Med Wochenschr 1995 Mar 11;125(10):467-74

[Lung disorders due to metals].

[Article in German]

Ruegger M

Abteilung Arbeitsmedizin, Schweizerische Unfallversicherungsanstalt Luzern.

Though metals represent the largest group of elements they rather rarely cause respiratory diseases. This article will therefore review the most important ones caused by inhaled dusts of metals and some of their inorganic compounds, but leaving aside **silicosis** and silicatosis as well as iatrogenically induced metal pneumopathies. Among toxic inflammatory diseases metal fume fever, an influenza-like condition caused by zinc oxide, ranks as the commonest. Activities such as **oxi-acetylene cutting and welding of zinc** covered metal pieces account for about 90% of all cases compensated in Switzerland. Due to the non-recurrent character of this type of work, the typical waning of symptoms while exposure is going on has become seldom. Toxic pneumonia caused by inhaled metal fumes occurs rather seldom. However, serious cases have been reported where soldiers were exposed to zinc chloride from smoke bombs. The existence and extent of chronic airflow limitation due to occupational exposure to metallic dusts have not been widely examined but are to be assumed when there is poor occupational hygiene. **Concerning asthma, there are at least four metals and several of their compounds which have been proven to cause variable airway narrowing, namely chromium, nickel, platinum and cobalt (the latter as hardmetal).** Platinum complex salts (chloro-compounds) are very potent sensitizers leading to a notable prevalence of asthma among exposed workforces. Nevertheless, there have been no such cases in Switzerland for more than ten years. **Hard-metal not only causes asthma but also an alveolitis-like interstitial lung disease progressing to fibrosis.**

D-penicillamine is a copper chelating drug.

Rev Rhum Mal Osteoartic 1986 Jan;53(1):15-20

[D-penicillamine: mechanism of cellular action and induced autoimmune diseases].

[Article in French]

Meyer O

The fall in the IgM rheumatoid factors under treatment is not sufficient to explain the effectiveness of D-penicillamine in rheumatoid arthritis. The mechanism of action of D-penicillamine is still poorly elucidated. In vitro, in the presence of copper ions, D-penicillamine inhibits the lymphoblastic transformation induced by polyclonal mitogens; it decreases the production of immunoglobulins by lymphocytes stimulated by the Pokeweed mitogen. This inhibitory action is exerted on the helper T lymphocytes via the production of hydrogen peroxide (H₂O₂). Monocytes are capable of blocking the inhibitory action of D-penicillamine. The mechanism of the auto-immune complications induced by D-penicillamine is controversial. Two theories have been proposed:--a modification of the auto-antigens due to the presence of the highly reactive thiol group;--an interference with the lymphoid cells involved in suppressor or effector lymphocyte cellular co-operation. **These auto-immune complications can be classified into two groups: organ-specific diseases such as myasthenia, polymyositis, thyroiditis, and non organ-specific diseases such as Sjogren's syndrome and lupus. The suspension of D-penicillamine generally leads to the resolution of the symptoms,** but corticosteroid and immunosuppressant treatment is sometimes required.

The following study shows that beer mitigates some of the effects of copper deficiency. Copper deficient rats given beer lived six times as long as copper deficient rats given water. Interestingly, the effects were found to be unrelated to the copper, chromium, and alcohol in the beer. My guess is that the effect is due to the yeast which other studies show increases copper uptake in the cells.

Am J Clin Nutr 1990 May;51(5):869-72

Beer mitigates some effects of copper deficiency in rats.

Klevay LM, Moore RJ

Because of an epidemiologic association of decreased risk of death from ischemic heart disease with moderate use of alcoholic beverages, and because numerous abnormalities found in people with ischemic heart disease are also found in animals deficient in copper, rats were fed a diet deficient in copper and were given either beer or water to drink. Rats drinking beer lived nearly six times as long and had lower plasma cholesterol, less cardiac enlargement, and higher liver copper. Apparent absorption and biological half-life of oral radiocopper were increased by beer. The effects were not attributable to alcohol, chromium, or copper in beer. Beer intakes were similar to those of some people in the United States. Results may explain seasonal cycles in plasma cholesterol and may be germane to the epidemiology of ischemic heart disease because diets in the United States seem to be low in copper.

Copper deficiency in rats causes increased serum levels of T3:

Title

Concentrations of thyroid hormones in serum and activity of hepatic 5' monodeiodinase in *copper*-deficient rats.

Author

Kralik A; Kirchgessner M; Eder K

Address

Institut für Ernährungsphysiologie, Technische Universität München, Freising-Weihenstephan.

Source

Z Ernährungswiss, 35(3):288-91 1996 Sep

Abstract

The aim of the present study was to investigate the effect of *copper* deficiency on thyroid hormone metabolism in rats. Therefore, an experiment with growing male Sprague-Dawley rats was carried out, consisting of two groups of rats fed either a *copper*-deficient (0.06 mg Cu/kg) or a *copper*-adequate diet (16 mg Cu/kg). Both groups of rats were fed identical quantities of diet by pair-feeding. *Copper* deficiency decreased the final body weight of the rats by 5% compared to *copper*-adequate control rats. A severe *copper*-deficient state in the rats fed the *copper*-deficient diet was proved by a large decrease of ceruloplasmin activity in serum (by 97%) and hematological changes. For estimation of thyroid hormone metabolism, the concentrations of total and free thyroxine (T4) and triiodothyronine (T3) in serum and the activity of hepatic 5' monodeiodinase (5'D) were determined. *Copper*-deficient rats had an increased concentration of T3 in serum, whereas the concentrations of total and free T4 as well as the activity of hepatic 5'D were not different compared with *copper*-adequate control rats. Therefore, the study shows that *copper* deficiency has only slight effects on thyroid hormone metabolism in growing rats.

Copper deficiency enhances the effects of PTU-induced hypothyroidism.

Title

Interrelationships between athyroidic and *copper*-deficient states in rats.

Author

Oliver JW

Source

Am J Vet Res, 36(11):1649-53 1975 Nov

Abstract

Possible interrelationships of *copper*-deficient (*copper*-deficient ration) and hypothyroid (thiouracil treatment) states in rats were examined. Clinical signs, necropsy changes, and thyroxine concentrations were determined in 6 groups of rats treated as follows: group A--nontreated control; group B--thiouracil treated; group C--fed *copper*-deficient ration; group D--thiouracil treated and fed *copper*-deficient ration; group E--thyroid-stimulating hormone (TSH) treated; and group F--TSH treated and fed *copper*-deficient ration. Clinical signs occurred first and were most severe in the thiouracil-treated rats fed *copper*-deficient ration and included conformational changes and slower maturation, weakening of ear cartilage, middle ear changes (reflected by tilting of heads), and alopecia. Fatty infiltration of hepatic tissue was found in all rats fed *copper*-deficient rations, and considerable fluid retention occurred in rats fed *copper*-deficient ration and subjected to daily TSH treatment. Adrenal gland weights were 81% of control values (adjusted for body weight) in thiouracil-treated rats fed *copper*-deficient ration, and hypophysis weights were 114 and 154% of control values in thiouracil-treated rats and thiouracil-treated rats fed *copper*-deficient ration, respectively. Thyroid gland weights were 281% of control values in both thiouracil-treated rats and thiouracil-treated rats fed *copper*-deficient ration. Plasma thyroxine concentrations were markedly reduced (9% of control value) in thiouracil-treated rats fed *copper*-deficient ration. Thus, *copper*-deficient and hypothyroid states were considerably enhanced when the 2 existed concurrently, giving added meaning and necessity to close surveillance of trace mineral concentrations and thyroid gland status.

Copper controls the DNA encoding of the thyroid hormone receptor.

Title

In vivo expression of rat liver c-erbA beta thyroid hormone receptor in yeast (*Saccharomyces cerevisiae*).

Author

Lu C; Yang YF; Ohashi H; Walfish PG

Address

Thyroid Research Laboratory, Samuel Lunenfeld Research Institute of Mt. Sinai Hospital, University of Toronto, Ontario, Canada.

Source

Biochem Biophys Res Commun, 171(1):138-42 1990 Aug 31

Abstract

To study thyroid hormone receptor (TR), we developed an in vivo expression system in yeast by using *acopper*-responsive yeast

metallothionein promoter and ubiquitin-fusion protein technology. The cDNA encoding full-length rat liver TR beta was expressed under the control of *copper*. The [¹²⁵I]T3 binding activities to yeast extracts were significantly correlated with the added *copper* sulfate into the medium. Partially purified TR from the transformed yeast had a high hormone binding affinity (K_d = 0.34) for T3 and could bind thyroid hormone response element in gel retardation analysis.

Copper-zinc superoxide dismutase (cu,zn-SOD)

Title

Localization of Cu/Zn and Mn superoxide dismutase in various thyroid disorders.

Author

Iwase K; Nagasaka A; Kato K; Ohtani S; Tsujimura T; Inagaki A; Jimbo S; Nakai A; Masunaga R; Hamada M; et al

Address

Department of Surgery, Fujita Health University School of Medicine, Toyoake, Japan.

Source

Acta Endocrinol (Copenh), 129(6):573-8 1993 Dec

Abstract

The intracellular localization of Cu/Zn- and Mn-superoxide dismutase (SOD), which catalyze the dismutation of superoxide radicals (O₂⁻) to O₂ and H₂O₂, was studied in the thyroid tissue of various thyroid disorders by an immunohistochemical technique. The concentrations of both SODs in those tissues were measured also by a sandwich enzyme immunoassay technique. *Copper*/zinc-SOD in thyroid tissues were identified by immunocytochemical staining in most cases of papillary carcinoma and in some cases of other thyroid disorders. In normal follicular cells this enzyme is localized in the perinuclear cytoplasm, whereas in thyroid tumor or hyperplastic follicular cells it exists homogeneously in cytoplasm. Manganese-SOD stained strongly in papillary carcinoma and papillary-growing cells in the thyroid tissue of adenoma and Graves' disease. The concentrations of Cu/Zn- and Mn-SOD in thyroid tumor tissues and hyperplastic follicular disorders were significantly higher than those in normal thyroid tissue when they were compared as a function of protein or deoxyribonucleic acid contents. The ratio of Mn-SOD to Cu/Zn-SOD was significantly higher only in papillary carcinoma, except for other thyroid disorders as compared with that in the normal thyroid. In conclusion, SOD seems to be related to cell proliferation and differentiation in the thyroid follicular cell because Cu/Zn-SOD changes its localization in tumor and hyperplastic follicular cells and because the Mn-SOD concentration is increased in papillary carcinoma or papillary-growing cells.

Diamine oxidase (and monamine oxidase) are copper containing enzymes which deaminate (break down) chemicals in the body.

Title

Putrescine metabolism and the study of diamine oxidase activity in vivo.

Author

Sourkes TL; Missala K

Source

Agents Actions, 11(1-2):20-7 1981 Apr

Abstract

The catabolism of ¹⁴C-putrescine (1,4-tetramethylene-diamine) to labeled CO₂ in small laboratory animals has been studied extensively in order to establish the influence of nutritional, endocrine and other factors on this process. Special attention has been paid to treatments that are known to affect the activity of diamine oxidase (DAO, histaminase, EC, 1.4.3.6), a *copper*-containing enzyme characteristically inhibited by semicarbazide. Thus, *copper*-deficient rats metabolize putrescine more slowly than their controls. Antimalarial drugs that inhibit histamine N-methyltransferase also inhibit putrescine catabolism in vivo and DAO activity in vitro. Adrenalectomized rats metabolize the diamine at a reduced rate, a result consistent with the previously demonstrated decrease of DAO in the tissues of several species of animal. There is no effect on the rate of catabolism of putrescine when thyroid state is altered. Heparin (up to 15,000 U/kg), which releases DAO from the small (0.1 mg/kg), intestine, and aminoguanidine (0.1 mg/kg), which inhibits the enzyme powerfully, both cause decreased rates of catabolism of the diamine in rats. The putrescine-catabolizing ability returns with a half-time of recovery of 15-18 h, corresponding to the estimates of SHAFF and BEAVER [36] for recovery of intestinal DAO activity following administration of heparin or cycloheximide. Together with our other results this suggests that what is being measured by putrescine catabolism depends to a significant extent on the activity of DAO in vitro.

Copper catalyzes LDL oxidation.

Title

Inhibition of low density lipoprotein oxidation by thyronines and probucol.

Author

Hanna AN; Feller DR; Witiak DT; Newman HA

Address

Department of Pathology, College of Medicine, Ohio State University, Columbus 43210.

Source

Biochem Pharmacol, 45(3):753-62 1993 Feb 9

Abstract

Oxidation of low density lipoproteins (LDL) results in increased macrophage uptake of LDL which may contribute to the formation of macrophage-derived foam cells in the early atherosclerotic lesion. In this study we show that thyroxine (T₄), its optical antipodes, certain desiodo analogs and probucol inhibited cupric sulfate-catalyzed oxidation of human LDL in a concentration-dependent manner as assessed by measuring the electrophoretic mobility, thiobarbituric acid reactive substances (TBARS) and LDL degradation in mouse macrophages. In Cu(2+)-catalyzed LDL oxidation at 24 hr, the TBARS level was 80 nmol/mg LDL protein/24-hr incubation. The concentrations (microM) of each agent producing 50% inhibition in the formation of oxidized LDL (IC₅₀) for TBARS, electrophoretic mobility and macrophage degradation, respectively, were 1.13, 1.27 and 1.30 for reversed triiodothyronine; 1.33, 1.80 and 1.27 for triiodothyronine; 1.33, 1.37 and 1.37 for racemic thyroxine, DL-T₄; 1.10, 1.40 and 1.50 for L-T₄; 1.13, 1.33 and 1.23 for D-T₄; and 1.47, 1.63 and 1.37 for probucol. No differences in inhibitory potency were observed when rT₃, T₃, the optical antipodes of T₄ and the hydrophobic antioxidant drug probucol were compared. In air-induced LDL oxidation, TBARS was 16.1 nmol/mg LDL protein/6-hr incubation. The IC₅₀ concentrations (microM) for TBARS and diene conjugation, respectively, were 0.187 and 0.336 for D-T₄; 0.205 and 0.243 for L-T₄ and 1.30 and 3.02 for probucol. With air-induced LDL oxidation conditions, the L-T₄ concentrations included the physiological range, and thyroid-binding globulin did not modify the inhibitory effect of the endogenous enantiomer, L-T₄. Putative uptake of this stereoisomer into LDL inhibited oxidation of these lipoproteins.

Since concentrations of these thyronines which blocked air-induced LDL oxidation were in the physiological range, we conclude that thyronines, like the pharmacological agent probucol, limit the oxidative modification of LDL and thus may serve as natural inhibitors of atherogenesis.

Copper protects against osteoporosis.

Title

[Effects of essential trace elements on bone turnover--in relation to the osteoporosis]

Author

Okano T

Address

Department of Hygienic Sciences, Kobe Pharmaceutical University.

Source

Nippon Rinsho, 54(1):148-54 1996 Jan

Abstract

Trace Elements are essential for normal growth and development of skeletons in humans and animals. Although they are minor building components in teeth and bone, they play important functional roles in bone metabolism and bone turnover. Fluoride accumulates in new bone formation sites and results in a net gain in bone mass. Aluminum induces impairment of bone formation by the inhibition of osteoblastic function. Magnesium enhances bone turnover by through the stimulation of osteoclastic function. Zinc regulates secretion of calcitonin from thyroid gland and influences on bone turnover. Gallium suppresses bone turnover in humoral hypercalcemia of malignancy in a similar mechanism as aluminum and cadmium. **Copper induces low bone turnover by both suppressions of osteoblastic and osteoclastic functions.** Iodine as the hormonal forms of thyroxine and triiodothyronine enhances bone turnover. **Among the trace elements in bone and hair, significant differences were found in the contents of zinc, copper and manganese between normal subjects and osteoporotic patients.** However, exact involvements of the trace elements in osteoporosis have not yet been clarified.

Copper requirement is higher with dietary fructose than with dietary starch.

Copper deficiency reduces immune system function. Immune system dysfunction created by excess dietary copper is restored by dietary zinc.

Vitamin A increases serum copper levels.

Title

[Effect of acute hypervitaminosis A on serum concentrations of Na, K, Mg, Fe, Zn and Cu in rats]

Author

Alarcón OM; Burguera JL; Burguera M

Address

Departamento de Bioquímica, Facultad de Medicina, Universidad de Los Andes, Mérida, Venezuela.

Source

Arch Latinoam Nutr, 37(2):305-11 1987 Jun

Abstract

The effect of hypervitaminosis A on the content of sodium, potassium, magnesium, iron, **zinc** and copper in rat serum was studied. Results were compared to findings in non-treated animals. The serum content of potassium, magnesium and copper increased significantly, while the content of sodium, **zinc** and iron decreased significantly in the treated animals, when compared to the values obtained with untreated animals. Possible mechanisms for these changes are discussed, and we conclude that high doses of vitamin A cause a marked change in the serum content on the measured cations.

Ocular copper deposition in lens:

Title **Ocular copper deposition associated with benign monoclonal gammopathy and hypercupremia.**

Author Probst LE; Hoffman E; Cherian MG; Yang J; Feagan B; Adams P; Nichols B

Address Department of Ophthalmology, University Hospital, University of Western Ontario, London, Canada.

Source Cornea, 15(1):94-8 1996 Jan

Abstract

The deposition of copper on Descemet's membrane and the anterior and posterior lens capsule with extreme hypercupremia and IgG hypergammaglobulinemia has been previously described with multiple myeloma and pulmonary carcinoma. **A 66-year-old man presenting with blurred vision was found to have bilateral golden-brown metallic dust-like deposits on the central region of Descemet's membrane and the anterior and posterior lens capsule. Laboratory investigations revealed an elevated serum copper level 10 times the normal level associated with a monoclonal gammopathy and a normal ceruloplasmin**

Copper binding to the serum proteins was investigated by three biochemical methods.

The results demonstrated that the major copper binding fraction in the serum was **IgG**. N-terminal amino acid analysis of the **IgG** did not find the sequence of Asp-Ala-His, which has been shown to be a copper binding site in albumin. This is the first report of benign monoclonal gammopathy being associated with the ocular deposition of copper.

Title

Suboptimal levels of dietary copper vary immunoresponsiveness in rats.

Abstract

The effects of severe, moderate, and mild copper deficiencies on cellular and humoral immunity were studied. Fifty male Sprague-Dawley rats, 5 wk of age, were fed diets containing 0.5, 2.0, 3.5, or 5.0 micrograms Cu/g for either 4 or 8 wk. Ten of the rats were fed the control diet, but were pair-fed with the 0.5-micrograms/g treatment group. All rats were immunized once with sheep red blood cells. Mean plasma-copper concentration reflected the dietary levels of copper, and ceruloplasmin activity correlated highly to plasma copper. Rats consuming suboptimal levels of copper responded differently to the deficiencies, so copper status varied among those animals. After 8 wk, cell proliferation, when stimulated by phytohemagglutinin, was dependent on the copper status of the animal. Severely deficient rats had consistently lower lymphocyte stimulation indexes for phytohemagglutinin and concanavalin A, but specific antibody response was not reduced. Immunoglobulin G (**IgG**) concentrations were variable for all rats, and immunoglobulin M (IgM) concentrations were lower for the severely deficient rats.

Title: **Specific cleavage of immunoglobulin G by copper ions.**

Author

Smith MA; Easton M; Everett P; Lewis G; Payne M; Riveros-Moreno V; Allen G

Address

Biotechnology Development Laboratories, Wellcome Research Laboratories, Beckenham, Kent, UK.

Source

Int J Pept Protein Res, 48(1):48-55 1996 Jul

Abstract

The hinge region of a recombinant-DNA-produced human IgG1 (Campath 1H) is specifically cleavable at a single copper-sensitive peptide bond, yielding a distinct fragment resolved by size-exclusion high-performance liquid chromatography. This novel metal ion-catalysed cleavage at slightly alkaline pH is inhibited by EDTA and its rate is reduced at slightly acidic conditions (pH 5-6) and accelerated by increasing concentrations of cupric ion and higher temperature. Complete cleavage was observed after incubation at pH 8 for 24 h with 1 mM CuCl₂. Sequence analysis determined the cleavage site to be the Lys226-Thr227 bond in the hinge-region sequence DKTHT. Cleavage of other IgGs was observed to varying degrees, and specific cleavage of synthetic peptides containing this pentapeptide sequence was also observed.

Title

Copper deficiency during perinatal development: effects on the immune response of mice.

Abstract

Dietary copper (Cu) was restricted in Swiss albino mice during five discrete intervals over a 9-wk period of perinatal development: gestation only (G), lactation only (L), 3 wk postlactation (PL), 1 wk after birth through postlactation (2/3L + PL), and lactation plus postlactation (L + PL). Biochemical and immunological status of mice in copper-deficient (-Cu) treatment groups in models G and L did not differ from that of copper-adequate (+Cu) controls. Signs of severe copper deficiency, such as low liver copper levels, and significant reductions in activity of plasma ceruloplasmin and splenocyte Cu-Zn superoxide dismutase were most evident in 6-wk-old mice from two groups, -Cu 2/3L + PL and -Cu L + PL. **Mice in these groups were anemic and had small thymuses and enlarged spleens compared to controls receiving +Cu treatment. The -Cu mice demonstrated impaired antibody (plaque-forming cells, PFC) response to sheep erythrocytes, and the attenuation was proportional to copper deficiency, as judged by liver copper levels.** Total plasma IgM levels were not greatly altered by -Cu treatment except in model L + PL. Total IgG levels were markedly reduced in this group and in the -Cu 2/3L + PL group. The PFC response of mice in the -Cu PL group was normal even though signs of copper deficiency were evident; however, the PFC response was reduced when -Cu treatment was extended to 5 wk and was reversible by switching to +Cu treatment. Splenocyte reactivity to B- and T-cell mitogens was not greatly different between groups. Incorporation of thymidine into DNA in the absence of mitogen was higher in -Cu mice. **It is evident that severity of copper deficiency is related to degree of impaired immunity.** Furthermore, severity of copper deficiency is dependent on duration and time of initiation of dietary copper restriction.

Title **The effects of copper deficiency with or without high dietary iron or molybdenum on immune function of cattle.**

Author

Ward JD; Gengelbach GP; Spears JW

Address

Department of Animal Science and Interdepartmental Nutrition Program, North Carolina State University, Raleigh 27695-7621, USA.

Source

J Anim Sci, 75(5):1400-8 1997 May

Abstract

Two experiments were conducted to determine the effects of Cu deficiency with or without high dietary Mo or Fe on the specific immunity of calves. In Exp. 1, calves from 38 bred heifers, fed corn silage-based experimental diets from the last third of gestation until the calves were weaned, were used. Dietary treatments were control (no supplemental Fe, Mo, or Cu), 600 mg of supplemental Fe/kg of DM, 5 mg of supplemental Mo/kg of DM, and 10 mg of supplemental Cu/kg of DM. In Exp. 2, 18 Holstein bull calves were fed commercial milk replacer low in Cu for 49 d and then fed semipurified diets containing approximately 1.1 mg of Cu/kg of DM or diets supplemented with 5 mg of Mo or 10 mg of Cu per kilogram of DM for 126 d. Feeding diets not supplemented with Cu resulted in severe Cu deficiency in both experiments. During Exp. 1, control calves had higher ($P < .10$) secondary antibody response to pig erythrocytes than Cu-, Mo-, and Fe-supplemented calves. During Exp. 2, in vitro Cu supplementation decreased ($P < .01$) lymphocyte blastogenic response. In vivo cell-mediated response to phytohemagglutinin was decreased ($P < .10$) by Cu supplementation during Exp. 1 but was increased ($P < .10$) by Cu and Mo supplementation during Exp. 2. Copper deficiency and Cu deficiency coupled with high dietary Mo or Fe produced inconsistent immune function responses, indicating that Cu deficiency may not affect specific immune function of calves.

Title: **Specific cleavage of histidine-containing peptides by copper(II), including tyrosine and IgG.**

Author

Allen G; Campbell RO

Address

Core Support Group, Wellcome Research Laboratories, Beckenham, Kent, UK.

Source

Int J Pept Protein Res, 48(3):265-73 1996 Sep

Abstract

Copper(II) cleaves with moderate specificity peptides containing Ser-His or Thr-His sequences, at the N-terminal side of the hydroxyaminoacyl residue. The reaction is slow, and is first-order in peptide: CuII complex, with a half-life of several hours at 62 degrees C in sodium bicarbonate buffer, pH 8. Cleavage of other histidine-containing peptides also occurs, at a rate around 10-100-fold less. EDTA completely quenches the cleavage. The reaction is stoichiometric in CuII and is inhibited by amine-containing buffer components; Tris at 19 mM inhibits cleavage by 50%. The reaction has a complex pH-dependence, being very slow below pH 5, and with rates increasing with pH from pH 7 to pH 9.5. Slower degradative side reactions do occur, with destruction of tyrosine residues, particularly in the presence of high concentrations of chloride ion, but the specific cleavage appears to be a hydrolysis, as determined by amino-acid analysis and mass spectrometry of the products. The cleavage is clearly different from the previously described oxidative degradation of proteins catalysed by copper ions. Cleavage of denatured IgG protein occurs with sufficient specificity to reveal distinct bands on SDS-polyacrylamide gel electrophoresis under reducing conditions.

Copper deficiency contributes to osteoporosis.

Title

Lack of a recommended dietary allowance for copper may be hazardous to your health.

Author

Klevay LM

Address

United States Department of Agriculture, Grand Forks Human Nutrition Research Center, North Dakota 58202-9034, USA.

Source

J Am Coll Nutr, 17(4):322-6 1998 Aug

Abstract

The 10th edition of Recommended Dietary Allowances (RDA) did not include an RDA for copper; rather a safe and adequate daily intake was suggested. Criteria, history and uses of RDAs were summarized along with data on dietary intakes, balance and depletion experiments, low (fats and oils, skim milk and yogurt) and high (legumes, mushrooms, nuts and seeds) copper foods and hazards of zinc supplements. Bone disease and cardiovascular disease from diets-low in copper have been studied in animals for decades. Men and women fed diets close to 1 mg of copper per day, amounts quite frequent in the US, responded similarly to deficient animals with reversible, potentially harmful changes in blood pressure control, cholesterol and glucose metabolism, and electrocardiograms. **Women supplemented with trace elements including copper experienced beneficial effects on bone density. These data exceed similar data on magnesium, selenium and zinc and are sufficient for establishing an RDA. Ischemic heart disease and osteoporosis are likely consequences of diets low in copper.** Numerous anatomical, chemical and physiological similarities between animals deficient in copper and people with ischemic heart disease have been noticed. Association between osteoporosis and low copper status deserves further inquiry. Augmenting low copper diets with high copper foods may be beneficial. Committees that establish RDAs should return to the traditions of the first nine editions and make recommendations that promote health and nutritional welfare, meet functional needs, prevent disease and promote public welfare.

Title

Interactions of vitamin C with lead and mercury.

Author

Hill CH

Source

Ann N Y Acad Sci, 355():262-6 1980

Abstract

Ascorbic acid has been found to interact with several elements in such a manner as to render them less available for animals. This property of the vitamin has a negative effect on the animals fed a copper-deficient diet, but a positive effect on those fed toxic levels of copper, selenium, vanadium, and cobalt. The effect of ascorbic acid in alleviating cadmium toxicity has been attributed to the effect of the vitamin on iron metabolism, since ferrous iron will also alleviate cadmium toxicity in the Japanese quail. The results of studies reported here indicate that iron will alleviate lead toxicity but ascorbic acid is ineffective. **Ascorbic acid will alleviate mercury toxicity, but iron exacerbates this condition.** For these two elements, the effects of iron and ascorbic acid are independent of each other.

Title

Effects of copper deficiency on the activity of the selenoenzyme glutathione peroxidase and on excretion and tissue retention of ⁷⁵SeO₃(2-).

Author

Jenkinson SG; Lawrence RA; Burk RF; Williams DM

Source

J Nutr, 112(1):197-204 1982 Jan

Abstract

Liver and lung activities of the antioxidant enzymes glutathione peroxidase (GSH-Px) and superoxide dismutase (SOD) were determined in control and *copper*-deficient rats. **Decreased activity of SOD was found in liver and decreased activity of the selenoenzyme GSH-Px was found in liver and lung in the copper-deficient animals.** The decreased liver activity of GSH-Px could be partially corrected by daily supplementation of the basal diet with sodium selenite. Urinary, fecal and biliary excretion of ⁷⁵SeO₃(2-) were determined in controls and *copper*-deficient rats in order to assess selenium losses. Urinary excretion of ⁷⁵Se was not different in the two groups. Fecal loss of ⁷⁵Se was increased in the *copper*-deficient animals when compared to controls and biliary excretion was decreased. Tissue retention of ⁷⁵Se was also determined in both groups. Retention of ⁷⁵Se in the *copper*-deficient rats was increased in brain and lung and decreased in liver. This pattern of tissue retention of ⁷⁵Se is similar to that which occurs in selenium-deficient rats. **Copper deficiency in rats results in decreased liver activity of both the copper-containing enzyme SOD and the selenoenzyme GSH-Px.** The mechanism of decreased GSH-Px activity is unknown.

Title

Development of copper deficiency in rats fed fructose or starch: weekly measurements of copper indices in blood.

Author

Fields M; Holbrook J; Scholfield D; Rose A; Smith JC; Reiser S

Source

Proc Soc Exp Biol Med, 181(1):120-4 1986 Jan

Abstract

Copper deficiency was induced in weanling rats fed diets whose sole source of carbohydrates was starch or fructose for 7 weeks. Conventional

parameters of *copper* status, plasma *copper* concentrations, ceruloplasmin activity, and erythrocyte superoxide dismutase (SOD) activity were longitudinally monitored weekly to follow the development of the deficiency and to correlate these indices with the degree of severity of the deficiency. **Although 30% of the rats fed a copper-deficient fructose diet died and no deaths occurred in rats fed the copper-deficient starch diet, plasma copper, ceruloplasmin, and SOD activities were reduced to a similar extent in all rats fed copper-deficient diets regardless of the type of dietary carbohydrate.** Thus, none of the indices used accurately reflected the greater degree of deficiency or mortality in rats fed the fructose diet deficient in *copper*. The results of the present study underscore the need for more sensitive tests or alternative parameters to assess *copper* status in living animals.

Title

Rat embryos cultured under copper-deficient conditions develop abnormally and are characterized by an impaired oxidant defense system.

Author

Hawk SN; Uriu-Hare JY; Daston GP; Jankowski MA; Kwik-Urbe C; Rucker RB; Keen CL

Address

Department of Nutrition, University of California, Davis 95616-8669, USA.

Source

Teratology, 57(6):310-20 1998 Jun

Abstract

Rat embryos (gestation days 9.0 and 10.0) obtained from dams that were fed a Cu-adequate (8 micrograms Cu/g) or Cu-deficient (< 0.5 micrograms Cu/g diet were cultured for 48 hr in Cu-adequate (16.2 microM) or Cu-deficient (1.0 microM) rat serum. Control embryos cultured in control serum were morphologically normal. Embryos from Cu-deficient dams developed abnormally when cultured in Cu-deficient serum; the abnormalities included distended hindbrains, blisters, blood pooling, and cardiac defects. Control embryos cultured in Cu-deficient serum and Cu-deficient embryos cultured in control serum also showed abnormal development, but to a lesser degree than that of the Cu-deficient embryos cultured in Cu-deficient serum. To test the idea that the above abnormalities were due in part to free radical induced damage occurring secondary to an impaired oxidant defense system, a chemiluminescence assay was used to detect superoxide dismutase (SOD) activity in the cultured embryos. **SOD activity was lowest in embryos cultured in Cu-deficient serum. When the Cu-deficient serum was supplemented with antioxidants (CuZnSOD or glutathione peroxidase), its teratogenicity was reduced. These data support the idea that an impaired oxidant defense system contributes to the dysmorphology associated with Cu deficiency. However, the Cu-deficient embryos also had low cytochrome c oxidase activity compared to control embryos--thus, multiple factors are likely contributing to Cu deficiency-induced abnormalities.**

Copper may be involved in migraine headaches.

Title

[Diet and migraine]

Author

Leira R; Rodr'iguez R

Address

Servicio de Neurolog'ia, Hospital General de Galicia Clinico Universitario, Santiago de Compostela.

Source

Rev Neurol, 24(129):534-8 1996 May

Abstract

Some foods in our diet can spark off migraine attacks in susceptible individuals. Some foods can bring an attack on through an allergic reaction. A certain number such as citrus fruits, tea, coffee, pork, chocolate, milk, nuts, vegetables and cola drinks have been cited as possible allergens associated with migraine. This mechanism has however been criticized: an improvement in symptoms by eliminating some food(s) from our diet does not necessarily mean an immunologically based allergic reaction. The high IgE incidence rate is not greater in such patients than in the population at large. Other allergic reactions unrelated to diet may also be associated with migraine attacks. On the other hand substances in food may be the cause of modifications in vascular tone and bring migraine on in those so prone. Among such substances are tyramine, phenylalanine, phenolic flavonoids, alcohol, food additives (sodium nitrate, monosodium glutamate, aspartame) and caffeine. Another recognized trigger for migraine is hypoglycemia. Such foods as chocolate, cheese, citrus fruits, bananas, nuts, 'cured' meats, dairy products, cereals, beans, hot dogs, pizza, food additives (sodium nitrate, monosodium glutamate in Chinese restaurant food, aspartame as a sweetener), coffee, tea, cola drinks, **alcoholic drinks such as red wine, beer or whisky distilled in copper stills, all may bring on a migraine attack.** For every patient we have to assess which foodstuffs are involved in the attack (not necessarily produced by consuming the product concerned) in order to try to avoid their consumptions as a means of prophylaxis for migraine.

Title

Dietary fructose but not starch is responsible for hyperlipidemia associated with copper deficiency in rats: effect of high-fat diet.

Author

Fields M; Lewis CG

Address

Nutrient Requirements and Functions Laboratory, Beltsville Human Nutrition Research Center, ARS, United States Department of Agriculture, Maryland 20705-2350, USA.

Source

J Am Coll Nutr, 18(1):83-7 1999 Feb

Abstract

OBJECTIVE: To test the hypothesis that *copper* deficiency in rats may be hyperlipidemic only when the diets consumed contain nutrients which contribute to blood lipids such as fructose and high fat. METHODS: Weanling male Sprague Dawley rats were fed diets which contained either starch or fructose as their sole carbohydrate source. The diets were either inadequate (0.6 microg Cu/g) or adequate (6.0 microg Cu/g) in *copper* and contained either high (300 g/kg) or low (60 g/kg) fat. At the end of the 4th week the rats were killed. Livers were analyzed for *copper* content. Plasma was analyzed for cholesterol and triglyceride concentrations. RESULTS: High-fat diet did not increase blood lipids in rats fed a *copper*-deficient diet containing starch. In contrast, the combination of high-fat diet with fructose increased blood triglycerides and fructose with *copper* deficiency resulted in a significant increases in blood cholesterol. CONCLUSIONS: **Hyperlipidemia of copper deficiency in rats is dependent on synergistic effects between dietary fructose and copper deficiency and fructose and amount of dietary fat. Hyperlipidemia does not develop if starch is the main source of dietary carbohydrate in a copper-deficient diet even if a high-fat diet is fed.**

Title

Decrease of cytochrome c oxidase protein in heart mitochondria of copper-deficient rats.

Author

Rossi L; Lippe G; Marchese E; De Martino A; Mavelli I; Rotilio G; Ciriolo MR

Address

Department of Biology, University of Rome Tor Vergata, Italy. rossil@utovrm.it

Source

Biometals, 11(3):207-12 1998 Sep

Abstract

Copper deficiency has been reported to be associated with decreased cytochrome c oxidase activity, which in turn may be responsible for the observed mitochondrial impairment and cardiac failure. We isolated mitochondria from hearts of *copper*-deficient rats: cytochrome c oxidase activity was found to be lower than in *copper*-adequate mitochondria. The residual activity paralleled *copper* content of mitochondria and also corresponded with the heme amount associated with cytochrome aa3. In fact, lower absorption in the alpha-band region of cytochrome aa3 was found for *copper*-deficient rat heart mitochondria. Gel electrophoresis of protein extracted from mitochondrial membranes allowed measurements of protein content of the complexes of oxidative phosphorylation, revealing a lower content of complex IV protein in *copper*-deficient rat heart mitochondria. The alterations caused by *copper* deficiency appear to be specific for cytochrome c oxidase. Changes were not observed for F0F1ATP synthase activity, for heme contents of cytochrome c and b, and for protein contents of complexes I, III and V. **The present study demonstrates that the alteration of cytochrome c oxidase activity observed in copper deficiency is due to a diminished content of assembled protein and that shortness of copper impairs heme insertion into cytochrome c oxidase.**

Title

Oxidant injury to hepatic mitochondria in patients with Wilson's disease and Bedlington terriers with copper toxicosis.

Author

Sokol RJ; Twedt D; McKim JM Jr; Devereaux MW; Karrer FM; Kam I; von Steigman G; Narkewicz MR; Bacon BR; Britton RS; et al

Address

Section of Pediatric Gastroenterology and Nutrition, University of Colorado School of Medicine, Denver.

Source

Gastroenterology, 107(6):1788-98 1994 Dec

Abstract

BACKGROUND/AIMS: Copper overload leads to liver injury in humans with Wilson's disease and in Bedlington terriers with copper toxicosis; however, the mechanisms of liver injury are poorly understood. This study was undertaken to determine if oxidant (free radical) damage to hepatic mitochondria is involved in naturally occurring copper toxicosis. **METHODS:** Fresh liver samples were obtained at the time of liver transplantation from 3 patients with Wilson's disease, 8 with cholestatic liver disease, and 5 with noncholestatic liver disease and from 8 control livers. Fresh liver was also obtained by open liver biopsy from 4 copper-overloaded and 4 normal Bedlington terriers and from 8 control dogs. Hepatic mitochondria and microsomes (humans only) were isolated, and lipid peroxidation was measured by lipid-conjugated dienes and thiobarbituric acid-reacting substances. In humans, liver alpha-tocopherol content was measured. **RESULTS:** Lipid peroxidation and copper content were significantly increased ($P < 0.05$) in mitochondria from patients with Wilson's disease and copper-overloaded Bedlington terriers. More modest increases in lipid peroxidation were present in microsomes from patients with Wilson's disease. Mitochondrial copper concentrations correlated strongly with the severity of mitochondrial lipid peroxidation. Hepatic alpha-tocopherol content was decreased significantly in Wilson's disease liver. **CONCLUSIONS:** These data suggest that the hepatic mitochondrion is an important target in hepatic copper toxicity and that oxidant damage to the liver may be involved in the pathogenesis of copper-induced injury.

Title

Low vitamin E content in plasma of patients with alcoholic liver disease, hemochromatosis and Wilson's disease [see comments]

Author

von Herbay A; de Groot H; Hegi U; Stremmel W; Strohmeyer G; Sies H

Address

Department of Medicine, University of D'usseldorf, Germany.

Source

J Hepatol, 20(1):41-6 1994 Jan

Abstract

The RRR-alpha-tocopherol (vitamin E) content in plasma from 46 patients with liver diseases and 23 healthy controls was determined by high performance liquid chromatography and electrochemical detection. Patients were divided into three groups: alcoholic liver diseases (n = 17; group A), hemochromatosis (n = 17; group B) and Wilson's disease (n = 12; group C). Lipid-standardized alpha-tocopherol levels were determined to neutralize differences due to hyperlipemia. The ratio of serum vitamin E to serum lipids (cholesterol, triglycerides, phospholipids) was highest in healthy controls and in patients in group A with cirrhosis and normal transaminases and bilirubin. Patients in group A with acute or chronic ethanol intoxication and high bilirubin levels had a 37% lower lipid-standardized vitamin E level than controls. Patients in group B with hemochromatosis, showing high serum iron (> 180 micrograms/dl), a low free iron binding capacity (< 8 mumol/l) and high ferritin-levels (< 450 micrograms/l), had a 34% lower vitamin E/lipid ratio than healthy controls. No significant lowering of the vitamin E/lipid ratio was observed in the other patients in group B. A significant decrease (37%) in the vitamin E/lipid ratio was only detectable in patients with Wilson's disease (group C) showing high free serum copper (> 10 micrograms/dl). The data support a role for free radicals in the pathogenesis of active liver diseases.

Title

Metabolism of 25-hydroxyvitamin D in copper-laden rat: a model of Wilson's disease.

Author

Carpenter TO; Pendrak ML; Anast CS

Address

Department of Medicine (Endocrinology), Children's Hospital, Boston, Massachusetts.

Source

Am J Physiol, 254(2 Pt 1):E150-4 1988 Feb

Abstract

Wilson's disease results in excess tissue accumulation of copper and is often complicated by skeletal and mineral abnormalities. We investigated *vitamin* D metabolism in rats fed a copper-laden diet rendering hepatic copper content comparable with that found in Wilson's disease. Injection of 25-hydroxyvitamin D3 [25(OH)D3] resulted in reduced 1,25-dihydroxyvitamin D [1,25(OH)2D] levels in copper-intoxicated rats. In vitro 25(OH)D-1 alpha-hydroxylase activity was impaired in renal mitochondria from copper-intoxicated animals. Activity was also inhibited in mitochondria from controls when copper was added to incubation media. **Impaired conversion of 25(OH)D to 1,25(OH)2D occurs in copper intoxication and suggests that altered vitamin D metabolism is a potential factor in the development of bone and mineral abnormalities in Wilson's disease.**

Title
Antioxidant enzyme gene transcription in copper-deficient rat liver.
Author
Lai CC; Huang WH; Klevay LM; Gunning WT 3rd; Chiu TH
Address
Department of Pharmacology, Medical College of Ohio, Toledo 43699-0008, USA.
Source
Free Radic Biol Med, 21(2):233-40 1996
Abstract

Antioxidant enzymes, Cu/Zn- and Mn-superoxide dismutase, *catalase*, and glutathione peroxidase, constitute an important defense mechanism against cytotoxicity of reactive oxygen species. Copper is essential for the activity of Cu/Zn-superoxide dismutase. Oxidative stress, therefore, is expected in organs of rats fed copper-deficient diet due to reduced Cu/Zn-superoxide dismutase activity. Our previous studies have shown that the expression of antioxidant enzymes was altered in copper-deficient rat liver. The present report was undertaken to study further the transcription of these enzymes in liver nuclei of rats made copper-deficient for 4 weeks. While copper deficiency decreased the copper in liver by about 80%, it did not alter the copper content in liver nuclei. In spite of a 100% elevation in nuclear iron concentration, liver nuclei from copper-deficient rats showed normal appearance. The transcriptional rates for Cu/Zn-superoxide dismutase, glutathione peroxidase, and glyceraldehyde-3-phosphate dehydrogenase were not altered by dietary copper deprivation. **In contrast, transcriptional rates for Mn-superoxide dismutase and beta-actin were increased but that for catalase was reduced in the nuclei isolated from the copper-deficient rat liver. These results suggest that oxidative stress, resulting from copper deficiency, differentially modulates the gene transcription for the antioxidant enzymes in rat liver.**

Title
Antioxidant defense system in lung of male and female rats: interactions with alcohol, copper, and type of dietary carbohydrate.
Author
Fields M; Lewis CG; Lure MD
Address
Beltsville Human Nutrition Research Center, US Department of Agriculture, Agricultural Research Service, MD 20705, USA.
Source
Metabolism, 45(1):49-56 1996 Jan
Abstract

Male and female rats were used to investigate the effects of type of dietary carbohydrate (CHO), copper, and ethanol consumption on lung antioxidant enzyme activities and levels of phosphorylated compounds in whole blood. **Copper-deficient female rats exhibited a greater degree of copper deficiency than males, as assessed by hepatic copper concentration and hepatic copper superoxide dismutase (CuSOD) activity. However, copper-deficient male rats fed fructose-containing diets exhibited greater growth retardation, anemia, and heart hypertrophy than females consuming the same diets and males fed starch.** In addition, one of 10 copper-deficient male rats that ate a fructose-based diet and drank water and one of 10 copper-deficient male rats that ate a starch-based diet and drank ethanol died. **Copper-deficient, starch-fed males exhibited the highest activities of glutathione peroxidase (GSH-Px) and catalase as compared with fructose-fed rats. Ethanol consumption elevated the activities of GSH-Px and catalase. Copper-deficient female rats exhibited higher catalase but lower GSH-Px activities than males. It is suggested that in copper deficiency, the ability to increase antioxidant enzyme activities in rats consuming starch is greater than in rats consuming fructose.** Rats fed starch are provided with a greater degree of protection against oxidative damage than rats fed fructose. In addition, polyphosphorylated compounds in blood were reduced in copper-deficient male rats that consumed fructose-based diets. This may impair supply of oxygen to tissues.

Title
Weak antioxidant defenses make the heart a target for damage in copper-deficient rats.
Author
Chen Y; Saari JT; Kang YJ
Address
Department of Pharmacology and Toxicology, University of North Dakota School of Medicine, Grand Forks 58202-9037.
Source
Free Radic Biol Med, 17(6):529-36 1994 Dec
Abstract

Copper deficiency causes more salient pathologic changes in the heart than in the liver of rats. Although oxidative stress has been implicated in copper deficiency-induced pathogenesis, little is known about the selective toxicity to the heart. Therefore, we examined the relationship between the severity of copper deficiency-induced oxidative damage and the capacity of antioxidant defense in heart and liver to investigate a possible mechanism for the selective cardiotoxicity. Weanling rats were fed a purified diet deficient in copper (0.4 microgram/g diet) or one containing adequate copper (6.0 microgram/g diet) for 4 weeks. Copper deficiency induced a 2-fold increase in lipid peroxidation in the heart (thiobarbituric assay) but did not alter peroxidation in the liver. The antioxidant enzymatic activities of superoxide dismutase, *catalase*, and glutathione peroxidase were, respectively, 3-, 50- and 1.5-fold lower in the heart than in the liver, although these enzymatic activities were depressed in both organs by copper deficiency. In addition, the activity of glutathione reductase was 4 times lower in the heart than in the liver. The data suggest that a weak antioxidant defense system in the heart is responsible for the relatively high degree of oxidative damage in copper-deficient hearts.

Title
Ultrastructure of hepatocytes in copper-deficient Sika deer (*Cervus nippon* Temminck).
Author
Seo H; Xie B; Wang S; Yoshikawa H; Oyamada T; Yoshikawa T
Address
Department of Veterinary Pathology, School of Medicine and Animal Sciences, Kitasato University, Japan.
Source
J Comp Pathol, 114(3):283-90 1996 Apr
Abstract

The livers of 13 Sika deer (*Cervus nippon* Temminck) aged 4 to 9 years and suffering from **copper deficiency (enzootic ataxia)** were examined histologically, histochemically and by electron microscopy. In addition, the serum and liver copper concentrations, measured in three animals, were found to be low. Histologically, the hepatocytes exhibited cloudy swelling, and numerous haemosiderin deposits were seen in the hepatocytes and Kupffer cells. Staining with p-dimethyl amino-benzylidene-rhodamine revealed distinctly fewer copper granules than normal. Histochemically, 3,3'-diaminobenzidine-H₂O₂ staining revealed increased numbers of *catalase*-positive granules around nuclei. Electron microscopically, "giant" and bizarre-shaped mitochondria, irregular depression of the mitochondrial membrane, and fusion of cristae were noted. Disorders of copper-containing enzymes, including cytochrome oxidase, caeruloplasmin and monoamine oxidase, may have been

responsible for the mitochondrial abnormalities.

Copper deficiency can cause a magnesium deficiency.

Title

Effect of copper-deficient diet on metabolism in rat auditory structures.

Author

Farms WB; Godfrey DA; Askari A

Address

Department of Otolaryngology, Medical College of Ohio, Toledo 43699-0008.

Source

Hear Res, 67(1-2):45-50 1993 May

Abstract

Copper is a trace element known to be critical for normal brain function, and abnormal copper metabolism has been associated with some disorders involving the auditory system. We examined effects of copper deficiency on metabolism in major structures of the auditory system. Homogenates of cochlea, cochlear nucleus and inferior colliculus of rats, as well as whole brain, were assayed for activities of enzymes of oxidative and glycolytic energy metabolism--malate and lactate dehydrogenase, enzymes of acetylcholine metabolism--choline acetyltransferase and acetylcholinesterase, and concentrations of amino acids. Whole brain was also assayed for activity of superoxide dismutase, a copper-containing enzyme, and concentrations of minerals. **For these chemicals and tissues, the only significant differences between copper-deficient and copper-adequate rats were: (1) decreased copper and magnesium and increased potassium concentrations in whole brain of copper-deficient rats and (2) an elevation of glutamine concentration in inferior colliculus and whole brain of copper-deficient rats.** The elevated *glutamine* could not be related to any change in activity of *glutamine* synthetase or glutaminase, major enzymes of *glutamine* metabolism. It is speculated that the increase in *glutamine* might result from a net increase in ammonia accumulation in the brains of copper-deficient rats.

Cooking foods in cans decreases available copper. This probably explains why cats fed canned fish and meat are more apt to get hyperthyroidism.

Am J Clin Nutr 2001 May;73(5):914-9

[Links](#)

Extent of thermal processing of infant formula affects copper status in infant rhesus monkeys.

Lonnerdal B, Kelleher SL, Lien EL.

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BACKGROUND: Infant rhesus monkeys are excellent models in which to study the effect of infant formulas on trace element absorption and status. Infants fed powdered formula from birth exhibit normal growth and have blood variables similar to those of breast-fed infants. **OBJECTIVES:** The objectives were to evaluate the effects of feeding ready-to-feed (RTF) formulas exposed to different heat treatments to infant monkeys, and, for one of these formulas, to compare the effect of fortification with 2 iron concentrations. **DESIGN:** From birth to age 5 mo, infant monkeys (n = 6/group) were fed one of the following formulas exclusively: 1) 12 mg Fe/L processed in cans (RTF-12), 2) formula in glass bottles with 12 mg Fe/L and manufactured by an ultrahigh-temperature (UHT) process (UHT-12), or 3) formula manufactured by a standard thermal process (STP), containing either 8 (STP-8) or 12 (STP-12) mg Fe/L. All formulas had similar copper concentrations (0.6 mg Cu/L). Anthropometric measures and venous blood samples were taken monthly. **RESULTS:** Weight and length gain did not differ among groups; however, the STP-12 group weighed less than the UHT-12 group at ages 2, 4, and 5 mo. Hemoglobin values were significantly lower in the RTF-12 group than in all other groups at ages 4 and 5 mo and serum ferritin was lower in the RTF-12 group than in the STP-12 group at age 5 mo. Copper status was lower in STP-12 infants than in STP-8 infants. There was a progressive and significant decline in plasma copper, ceruloplasmin, and Cu/Zn superoxide dismutase activity in infants fed canned formula (RTF-12). Furthermore, coat color changed from normal brown to silver. These outcomes suggest that the canned formula induced copper deficiency in infant monkeys. **CONCLUSIONS:** Excessive heat treatment of formula can have a pronounced negative effect on copper status. High iron concentrations did not improve iron status but may adversely affect copper status.

Title

Copper-glutathione complexes under physiological conditions: structures in solution different from the solid state coordination.

Author

Pederson JZ; Steinkühler C; Weser U; Rotilio G

Address

Department of Biology, University of Rome Tor Vergata, Italy.

Source

Biometals, 9(1):3-9 1996 Jan

Abstract

The physiologically important copper complexes of oxidized glutathione have been examined by electron spin resonance (ESR) spectroscopy in aqueous solution at neutral pH. Low temperature measurements show that the Cu(II) binding site in oxidized glutathione has

the same ligand arrangement as in copper complexes of S-methylglutathione, *glutamine*, glutamate and glycine. The site is composed of the amino nitrogens and the carboxyl oxygens of two gamma-glutamyl residues; there is no interaction with amide nitrogens, the sulphur bond or the glycyl carboxyl groups. At high metal to ligand ratios a binuclear species exists, in which each Cu(II) binds only to one gamma-glutamyl residue. The previously reported forbidden transition detected at $g = 4$ is due to non-specific aggregation and not to spin coupling of intramolecular sites. Liquid solution ESR spectra show the Cu(II)-glutathione complex has a lower mobility than the corresponding Cu(II)-S-methylglutathione species. From the degree of spectral anisotropy the complex with glutathione is calculated to exist as a dimer. These results demonstrate that the physiologically relevant complex between copper and oxidized glutathione in solution is completely different from the known solid state structure determined by crystallography.

Title

The role of glutathione in copper metabolism and toxicity.

Author

Freedman JH; Ciriolo MR; Peisach J

Address

Institute for Structural and Functional Studies, University City Science Center, Philadelphia, Pennsylvania 19140.

Source

J Biol Chem, 264(10):5598-605 1989 Apr 5

Abstract

Cellular copper metabolism and the mechanism of resistance to copper toxicity were investigated using a wild type hepatoma cell line (HAC) and a copper-resistant cell line (HAC600) that accumulates copper and has a highly elevated level of metallothionein (MT). Of the enzymes involved in reactive oxygen metabolism, only glutathione peroxidase was elevated (3-4-fold) in resistant cells, suggestive of an increase in the cellular flux of hydrogen peroxide. A majority of the cytoplasmic copper (greater than 60%) was isolated from both cell lines as a GSH complex. Kinetic studies of ^{67}Cu uptake showed that GSH bound ^{67}Cu before the metal was complexed by MT. Depletion of cellular GSH with buthionine sulfoximine inhibited the incorporation of ^{67}Cu into MT by greater than 50%. These results support a model of copper metabolism in which the metal is complexed by GSH soon after entering the cell. The complexed metal is then transferred to MT where it is stored. This study also indicates that resistance to metal toxicity in copper-resistant hepatoma cells is due to increases in both cellular GSH and MT. Furthermore, it is suggested that elevated levels of GSH peroxidase allows cells to more efficiently accommodate an increased cellular hydrogen peroxide flux that may occur as a consequence of elevated levels of cytoplasmic copper.

Title

Glutathione production in copper-deficient isolated rat hepatocytes.

Author

Chao PY; Allen KG

Address

Department of Food Science and Human Nutrition, Colorado State University, Fort Collins 80523.

Source

Free Radic Biol Med, 12(2):145-50 1992

Abstract

Dietary copper deficiency has been shown to reduce copper-dependent superoxide dismutase (SOD) activity and to increase lipid peroxidation in rats. Circulating reduced glutathione (GSH) concentrations are elevated in copper-deficient (CuD) rats, which suggests an increased GSH synthesis or decreased degradation, perhaps as an adaptation to the oxidative stress of copper deficiency. GSH synthesis was examined in isolated hepatocytes from CuD rats. Isolated hepatocytes were prepared by collagenase perfusion and incubated in Krebs-Henseleit bicarbonate buffer, pH 7.4, 10 mM glucose, 2.5 mM Ca^{2+} in the presence and absence of 1.0 mM buthionine sulfoximine (BSO), a specific inhibitor of GSH synthesis. Cell viability was assessed by trypan blue exclusion. GSH and oxidized *glutathione* (GSSG) were measured by the *glutathione* reductase recycling assay. Copper deficiency depressed hepatocyte Cu by greater than 90% and increased intracellular GSH by 41-117% over the 3-h incubation, with a two- to threefold increase in the rate of intracellular GSH synthesis. Intracellular GSSG values were minimally influenced by CuD, with a constant mol% GSSG. Extracellular total *glutathione* (GSH + 2GSSG) synthesis was increased by approximately 33%. Both intracellular GSH and extracellular total *glutathione* synthesis were inhibited by BSO. The pattern of food consumption in CuD rats, meal fed versus ad libitum fed, had no effect on *glutathione* synthesis. The results indicate an increased hepatic GSH synthesis as a response to dietary copper deficiency and suggest an interrelationship between the essential nutrients involved in oxyradical metabolism.

Title

Inhibition of elevated hepatic glutathione abolishes copper deficiency cholesterolemia.

Author

Kim S; Chao PY; Allen KG

Address

Department of Food Science and Human Nutrition, Colorado State University, Fort Collins 80523.

Source

FASEB J, 6(7):2467-71 1992 Apr

Abstract

Dietary copper deficiency causes hypercholesterolemia and increased hepatic 3-hydroxy-3-methyl-glutaryl coenzyme A (MHG-CoA) reductase activity and increased hepatic *glutathione* (GSH) in rats. We hypothesized that inhibition of GSH production by L-buthionine sulfoximine (BSO), a specific GSH synthesis inhibitor, would abolish the cholesterolemia and increased HMG-CoA reductase activity of copper deficiency. In two experiments, two groups of 20 weanling male rats were fed diets providing 0.4 and 5.8 micrograms Cu/g, copper-deficient (Cu-D) and copper-adequate (Cu-A), respectively. At 35 days plasma cholesterol was significantly elevated by 30 to 43% in Cu-D and 10 animals in each of the Cu-D and Cu-A groups were randomly assigned to receive 10 mM BSO solution in place of drinking water and continued on the same diets for another 2 wk. At necropsy Cu-D animals had a significant 52 to 58% increase in plasma cholesterol. BSO administration abolished the cholesterolemia in Cu-D rats, but had no influence on plasma cholesterol of Cu-A rats. Hepatic GSH was increased 39 to 82% in Cu-D rats and BSO abolished this increase. BSO was without effect on cardiac hypertrophy, plasma and liver copper, and hematocrit indices of copper status. Liver microsome HMG-CoA reductase activity was significantly increased 85 to 288% in Cu-D rats and BSO administration abolished this increase in activity in Cu-D rats. **The results suggest that copper deficiency cholesterolemia and elevated HMG-CoA reductase activity are a consequence of elevated hepatic GSH, and provide evidence for GSH regulation of cholesterol metabolism in intact animals.**

Title

The effects of selenium and copper deficiencies on glutathione S-transferase and glutathione peroxidase in rat liver.

Author

Arthur JR; Morrice PC; Nicol F; Beddows SE; Boyd R; Hayes JD; Beckett GJ

Address

Rowett Research Institute, Bucksburn, Aberdeen, U.K.

Source

Biochem J, 248(2):539-44 1987 Dec 1

Abstract

Selenium (Se) deficiency in rats produced significant increases in the activity of hepatic *glutathione* S-transferase (GST) with 1-chloro-2,4-dinitrobenzene as substrate and in various GST isoenzymes when determined by radioimmunoassay. These changes in GST activity and concentration were associated with Se deficiency that was severe enough to provoke decreases of over 98% in hepatic Se-containing *glutathione* peroxidase activity (Se-GSHpx). However, decreases in hepatic Se-GSHpx of 60% induced by copper (Cu) deficiency had no effect on GST activity or concentration. Increased GST activity in Se deficiency has previously been postulated to be a compensatory response to loss of Se-GSHpx, since some GSTs have a non-Se-*glutathione* peroxidase (non-Se-GSHpx) activity. However, the GST isoenzymes determined in this study, GST Yb1Yb1, GST YcYc and GST YaYa, are known to have up to 30-fold differences in non-Se-GSHpx activity, but they were all significantly increased to a similar extent in the Se-deficient rats.

Title

Role of cytosolic copper, metallothionein and glutathione in copper toxicity in rat hepatoma tissue culture cells.

Author

Steinebach OM; Wolterbeek HT

Address

Department of Radiochemistry, Delft University of Technology, The Netherlands.

Source

Toxicology, 92(1-3):75-90 1994 Sep 6

Abstract

Effects of metallothionein (MT) synthesis inhibiting compounds (actinomycin D, cycloheximide), MT synthesis stimulating compounds (dexamethasone, dibu-cAMP) and interfering metals (Cd, Zn) on *copper* accumulation were investigated in rat hepatoma tissue culture cells. *Copper*-metallothionein (Cu-MT) and MT-associated *copper* levels were determined to find a possible correlation between cytosolic *copper* concentrations and MT as a Cu-detoxifying protein. Further, intracellular non-MT associated *copper* levels and levels of GSH and SOD were determined. Cell viability was tested under all experimental conditions by measuring LDH-release, K⁺ uptake and total cell protein. Administration of dexamethasone and dibu-cAMP showed no effect on MT levels (compared with controls), and only a marginal effect on 64Cu and total Cu accumulation. Administration of actinomycin D resulted in increased *copper* accumulation in the particulate fraction, possibly due to inhibition of *copper* secretion processes and/or protein synthesis. Presence of zinc had no effect on MT levels nor on total Cu and 64Cu levels, in contrast with cadmium which drastically enhanced *copper* accumulation and MT levels in the cells. Cu/MT ratios varied from 1.0 +/- 0.3 to 3.3 +/- 1.2, which is far below the assumed maximum molar ratio of 8-12 mol Cu per mol MT. SOD levels appeared to be enhanced up to 2- or 3-fold in the presence of Cd²⁺, relative to control values. The role of GSH as Cu-intermediate in intracellular Cu distribution plus its role in *copper* defence mechanism(s) was tested by application of BSO, an inhibitor of GSH synthesis. It was found that BSO had no effect on intracellular MT level; it was found however that MT-bound *copper* levels were markedly decreased. The results presented support a model for *copper* metabolism in hepatoma tissue culture (HTC) cells, where Cu(I) is complexed by GSH immediately after entering the cell. GSH is capable of transferring *copper* to MT where it is stored. Depletion of GSH (by administration of Cd²⁺, actinomycin D, cycloheximide) almost instantaneously results in enhanced cellular toxicity. When also MT is depleted (by actinomycin D) non-MT associated, 'free' cytosolic Cu²⁺ is elevated, and HTC cells rapidly lose their resistance to *copper* toxicity, as also reflected in loss of cell viability (LDH, K⁺ and total cell protein).

Title

Dietary copper deficiency increases the mast cell population of the rat.

Author

Schuschke DA; Saari JT; West CA; Miller FN

Address

Center for Applied Microcirculatory Research, University of Louisville, Kentucky 40292.

Source

Proc Soc Exp Biol Med, 207(3):274-7 1994 Dec

Abstract

Mast cell-released histamine has been implicated in the enhanced acute inflammatory response of copper-deficient rats. The present study examined possible changes in the copper-deficient mast cell which may account for increased macromolecular leakage and edema formation. Mast cell populations were determined in the cremaster muscle of copper-adequate and copper-deficient rats. Total *histamine* content, unstimulated *histamine* release and concentration-dependent *histamine* release with the mast cell secretagogue compound 48/80 were also determined in isolated peritoneal mast cells. A significantly higher number of mast cells were found in the cremaster muscle of the copper-deficient rats (78 +/- 7 cells/5 microns section) than in the copper-adequate controls (51 +/- 4). Total *histamine* content per cell as well as unstimulated and stimulated release of the inflammatory mediator per cell were not different between the groups. The results suggest that dietary copper deficiency increases the mast cell population but does not alter the mast cell *histamine* content or sensitivity to degranulation in the rat. **This increase in the number of mast cells may be a mechanism by which acute inflammation is enhanced in copper deficiency.**

Title

Copper deficiency and posterior paralysis (Shalal) in small ruminants in the Sultanate of Oman.

Author

Ivan M; Hidirolou M; al-Ismaily SI; al-Sumry HS; Harper RB

Address

Animal Research Centre, Agriculture Canada, Ottawa, Ontario.

Source

Trop Anim Health Prod, 22(4):217-25 1990 Nov

Abstract

A **posterior ataxia** or paralysis in goats and sheep is a syndrome known as Shalal within the Sultanate of Oman. An investigation was carried out into the etiology of the syndrome. Samples of blood and tissues were obtained from normal and Shalal-affected goats and sheep. Samples of feed were collected from the affected areas of the Sultanate. Chemical analyses of samples showed that affected animals suffered from severe copper deficiency in spite of sufficient copper contents in feed. However, concentrations of sulphur and iron in the feed were high. **It was concluded that the Shalal syndrome in Oman is the condition generally known as swayback or enzootic ataxia caused by conditioned copper deficiency.** The deficiency is probably due to copper-sulphur and copper-iron interactions in the rumen, enhanced by

feeding of fresh roughage containing rumen degradable proteins.

Title

Molybdenum.

Author

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Source

J Toxicol Clin Toxicol, 37(2):231-7 1999

Abstract

Molybdenum does not exist naturally in the pure metallic form and of the 5 oxidation states (2-6) the predominant species are Mo(IV) and Mo(VI). Molybdenum rapidly polymerizes to a wide variety of complex polymolybdate compounds in solution. The vast majority of molybdenum is used in metallurgical applications (stainless steel, cast-iron alloys). Ammonium tetrathiomolybdate is an experimental chelating agent for Wilson's disease. For the general population, the diet is the most important source of molybdenum and concentrations in water and air usually are negligible. The average daily dietary intake is about 0.1-0.5 mg m.o. Molybdenum is an essential element with relatively low toxicity. Enzymes containing molybdenum catalyze basic metabolic reactions in the carbon, **sulfur**, and nitrogen cycles. Elimination of molybdenum occurs via the kidney and usually is complete within several weeks. **Molybdenosis (teart) is a form of molybdenum toxicity that produces a disease in ruminants similar to copper-deficiency.** Little data are available on the human toxicity of molybdenum. A gout-like syndrome and pneumoconiosis have been associated with excessive concentrations of molybdenum, but the inadequate design of the studies prevents an adequate determination of the etiology of these effects.

Title

Modification of vitamin A metabolism in rats fed a copper-deficient diet.

Author

Rachman F; Conjat F; Carreau JP; Bleiberg-Daniel F; Amedee-Manesme O

Address

INSERM U 56, Universit'e Paris-Sud, H^opital d'Enfants, Bic^etre, France.

Source

Int J Vitam Nutr Res, 57(3):247-52 1987

Abstract

The liver is the main storage site of vitamin A and copper. Inverse relationships between **copper** and vitamin A liver concentrations have been suggested. We have investigated the consequences of a **copper**-deficient diet on liver and blood vitamin A storage in Wistar rats. Animals were fed either a **copper**-deficient diet for 45 days from weaning, or an identical diet containing adequate amounts of **copper**. Concentrations of vitamin A were determined by isocratic high performance liquid chromatography using UV detection. We have observed in the liver of the rats fed a **copper**-deficient diet a significantly higher mean level of retinyl esters (148 +/- 37 micrograms/g of liver) and retinol (3.3 +/- 1.4 micrograms/g of liver) compared to the mean concentration of the retinyl esters (53 +/- 8.5 micrograms/g of liver) (p less than 0.01) and retinol (1.4 +/- 0.5 micrograms/g of liver) (p less than 0.01) in controls. Opposite results were observed in the serum of the group fed a **copper**-deficient diet as these rats had a significantly lower level of retinol (22 +/- 4 micrograms/100 ml) compared to the mean concentration in the controls (64 +/- 20 micrograms/100 ml) (p less than 0.01). **These findings suggest that a copper-deficient diet may cause defective transport of vitamin A from liver to blood.** This experimental model may be useful to further investigate unusual liver vitamin A and **copper** concentrations observed in children during various hepatobiliary diseases.

In Vivo 1989 Jul-Aug;3(4):285-93

Rhodium, iridium, copper and gold antitumor organometallic compounds (review).

Haiduc I, Silvestru C

Babes-Bolyai University, Chemistry Department, Cluj-Napoca, Romania.

Recent results on the antitumor activity of organometallic compounds of rhodium, iridium, copper and gold are reviewed. Coordination compounds of some organic ligands are also briefly mentioned. The most promising seem to be copper and gold complexes which exhibited remarkable activity against several tumor system.

J Med Invest 1999 Feb;46(1-2):29-33

Effects of vitamin E and vitamin C supplementation on plasma lipid peroxidation and on oxidation of apolipoprotein B-containing lipoproteins in experimental hyperthyroidism.

Dirican M, Tas S

Department of Biochemistry, Uludag University Medical School, Turkey.

Increasing numbers of experimental and epidemiological studies suggest the involvement of free radicals in the pathogenesis of various disease entities. Similarly, oxidative processes have been implicated as playing roles in the genesis of hyperthyroidism-induced damage. In this study, we investigated the effects of vitamin E and vitamin C on plasma lipid peroxidation and the susceptibility of apolipoprotein B (apo B)-containing lipoproteins to oxidation in experimental hyperthyroidism. The study animals were initially divided into a control group (Group C) and a hyperthyroid group. The latter was further re-grouped later according to their vitamin supplementation status: Hyperthyroid group without vitamin supplementation (Group H), hyperthyroid group with vitamin E supplementation (Group H+E) and hyperthyroid group with vitamin C supplementation (Group H+C). Malondialdehyde (MDA) level was measured as an indicator of plasma lipid peroxidation. The apo B-containing lipoproteins were separated by precipitation and incubated with copper sulphate. The MDA levels of this non-HDL fraction were measured prior to and after 1, 2 and 3 hours of incubation. Plasma MDA levels showed no significant differences among groups. Whereas MDA levels measured in non-HDL fraction were significantly higher in Group H than Group C. Group H+E and Group H+C had significantly lower MDA levels than Group H in all these measurements. This finding strongly indicates an increased susceptibility of apo B-containing lipoproteins to oxidation in hyperthyroidism, and that vitamin E as well as vitamin C supplementation protect these lipoproteins from copper-induced oxidation.

Putrescine metabolism and the study of diamine oxidase activity in vivo.

Sourkes TL, Missala K

The catabolism of 14C-putrescine (1,4-tetramethylene-diamine) to labeled CO₂ in small laboratory animals has been studied extensively in order to establish the influence of nutritional, endocrine and other factors on this process. **Special attention has been paid to treatments that are known to affect the activity of diamine oxidase (DAO, histaminase, EC, 1.4.3.6), a copper-containing enzyme characteristically inhibited by semicarbazide. Thus, copper-deficient rats metabolize putrescine more slowly than their controls.** Antimalarial drugs that inhibit histamine N-methyltransferase also inhibit putrescine catabolism in vivo and DAO activity in vitro. Adrenalectomized rats metabolize the diamine at a reduced rate, a result consistent with the previously demonstrated decrease of DAO in the tissues of several species of animal. There is no effect on the rate of catabolism of putrescine when thyroid state is altered. Heparin (up to 15,000 U/kg), which releases DAO from the small (0.1 mg/kg), intestine, and aminoguanidine (0.1 mg/kg), which inhibits the enzyme powerfully, both cause decreased rates of catabolism of the diamine in rats. The putrescine-catabolizing ability returns with a half-time of recovery of 15-18 h, corresponding to the estimates of SHAFF and BEAVEN [36] for recovery of intestinal DAO activity following administration of heparin or cycloheximide. Together with our other results this suggests that what is being measured by putrescine catabolism depends to a significant extent on the activity of DAO in vitro.

Nahrung 1988;32(8):755-65

The physiological role of copper and the problems of copper nutritional deficiency.

Wachnik A

National Institute of Food-Hygiene and Nutrition, Budapest, Hungary.

The paper deals with recent achievements concerning the physiological role of copper in the human organism. The problem of copper supplementation of the human diet is discussed. An outlook is given on the contemporary theories referring to the role of copper in nutrition. Special attention has been paid to the copper-containing enzymes and copper-dependent enzymes as well as to the problem of nutritional copper deficiencies. This paper shows the necessity of copper for: --"cleaning" of the organism from the excesses of free radicals, biogenic amines and cholesterol --the proper synthesis of hemoglobin, elastin, collagen and probably thyroid hormones --providing the energy formed in the respiratory chain and needed for biochemical syntheses and proper physical activity.

J Biol Inorg Chem 1999 Apr;4(2):145-53

Copper chaperones: function, structure and copper-binding properties.

Harrison MD, Jones CE, Dameron CT

National Research Centre for Environmental Toxicology, University of Queensland, Australia.

Copper is an absolute requirement for living systems and the intracellular trafficking of this metal to copper-dependent proteins is fundamental to normal cellular metabolism. The copper chaperones perform the dual functions of trafficking and the prevention of cytoplasmic exposure to copper ions in transit. Only a small number of copper chaperones have been identified at this time but their conservation across plant, bacterial and animal species suggests that the majority of living systems utilise these proteins for copper routing. The available data suggest that each copper-dependent protein in the cell is served by a specific copper chaperone. Although copper chaperones cannot be substituted for one another in a given cell type, copper chaperones that deliver to the same protein in different cell types appear to be functionally equivalent. The majority of the copper chaperones identified thus far have an "open-faced beta-sandwich" global fold with a conserved MXCXC metal-binding motif. Specificity for a given copper-dependent protein appears to be mediated by the residues surrounding the copper-binding motif. Copper binds to such proteins as Cu(I) in a trigonal complex with three sulfur ligands. Only the copper chaperone specific for cytochrome-c-oxidase, Cox17, deviates from this design.

Biofactors 1999;10(1):53-9

Copper and signal transduction: platelets as a model to determine the role of copper in stimulus-response coupling

Johnson WT

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Platelets from copper-deficient rats have been used as a model to investigate the role of copper in receptor-mediated cellular responses. Copper deficiency doubles the rate of dense granule secretion and increases myosin association with the platelet cytoskeleton following thrombin stimulation. Mechanisms underlying the effects of copper deficiency on thrombin-induced signals that elicit dense granule secretion involve suppression of protein kinase C activity and impairment of Ca²⁺ release from intracellular stores. Copper deficiency also reduces the cellular GTP content of platelets. This may limit receptor effector coupling through GTP-dependent regulatory proteins leading to protein kinase C activation and the release of Ca²⁺ from intracellular stores. The reduction in GTP content during copper deficiency results from its utilization to maintain cellular ATP levels in response to severely inhibited cytochrome c oxidase activity in platelet mitochondria. **Thus, the role of copper in maintaining normal signal transduction may be indirectly related to its biological function in mitochondria.**

Ann Nutr Metab 1986;30(5):335-44

Estimation of minerals and trace elements provided by beverages for the adult in France.

Darret G, Couzy F, Antoine JM, Magliola C, Mareschi JP

The total average amount of beverages absorbed daily (1,378 ml) is split up as follows: tap water (650 ml where from 170 ml are used for the preparation of coffee and tea); bottled water (190 ml); alcoholic drinks (481 ml) and soft drinks (57 ml). Under these conditions, the intake is estimated at (mg/day): Na: 50, K: 450, P: 83, Ca: 141, Mg: 54, Fe: 2.9, Zn: 0.64, Cu: 0.46, Mn: 0.40, F: 0.64, I: 0.09, Cr: 0.013, Se: 0.031. The

most significant supplies for both quantity and quality are those of calcium (18% of the needs), iron (29%), copper (19%), fluorine (24%) and magnesium (16%) for the adult. **Alcoholic drinks represent 35% of the daily intake of beverages; they are likewise the main source of minerals** such as: iodine and iron (wine), selenium (beer), fluorine, calcium and copper (in all alcoholic drinks). Calcium and fluorine are the main minerals provided by the different types of water. We have shown the influence of the geographical origin of the tap water on the Ca and F intake, as well as the influence of individual behavior with respect to the selection of his main drink.

Br Med Bull 1999;55(3):658-68

Thyroid function.

Arthur JR, Beckett GJ

Division of Micronutrient and Lipid Metabolism, Rowett Research Institute, Aberdeen, UK.

[Medline record in process]

Normal thyroid status is dependent on the presence of many trace elements for both the synthesis and metabolism of thyroid hormones. Iodine is most important as a component of the hormones, thyroxine and 3,3',5-tri-iodothyronine (T3) and iodine deficiency may affect approximately one billion people throughout the world. Selenium is essential for normal thyroid hormone metabolism being involved with selenium-containing iodothyronine de-iodinases that control the synthesis and degradation of the biologically active thyroid hormone, T3. Additionally, selenoperoxidases and thioredoxin reductase protect the thyroid gland from peroxides produced during the synthesis of hormones. The roles of iron, zinc and copper in the thyroid are less well defined but sub- or supraoptimal dietary intakes of all these elements can adversely affect thyroid hormone metabolism.

PMID: 10746354, UI: 20210449

Carl C. Pfeiffer, Ph.D., M.D.

UNSUSPECTED COPPER AND/OR ALUMINUM POISONING IN PATIENTS AND THE TREATMENT

Many patients have a low blood histamine (histapenia) & high serum copper level. Low histamine patients are typically overstimulated with thoughts racing through their minds making normal ideation difficult. Low histamine children are hyperactive while often healthy in other respects. Serum Cu levels in these patients are abnormally high. The normal level of serum Cu is about 100 mcg%. Since Cu is a brain stimulant and destroys histamine, the elevated serum (and presumably brain Cu) level probably accounts for many symptoms, including the low blood histamine level. The treatment Rx consists of the administration of zinc, manganese, vit. C, niacin, vit. B-12, and folic acid. Folic acid in conjunction with B-12 injections raises blood histamine while lowering the degree of symptomatology. Zn allows for the normal storage of histamine in both the blood cells and the brain. Zn and manganese increase the urinary excretion of copper. Patients with loss of memory frequently have high blood AL levels above 20 ppb. As magnesium, zn and vit C. are given the high blood AL level decreases to normal (less than 10 ppb) and memory improves. Accumulation of AL occurs in various human tissues including blood, brain, liver & bone. Several independent research reports now indicate that a high AL intake may have an adverse effect on memory in the adult (Alzheimer's D.), & may be a factor in learning disabilities & behavioral problems in younger people. Humans do not need AL for any purpose. Individuals with elevated blood AL levels, memory loss & those frequently exposed to AL compounds will find it beneficial to minimize or eliminate all AL sources.

Sci Total Environ 2000 Apr 17;249(1-3):143-70

Experimental copper and chromium deficiency and additional molybdenum supplementation in goats. II. Concentrations of trace and minor elements in liver, kidneys and ribs: haematology and clinical chemistry.

Frank A, Danielsson R, Jones B

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Since the mid-1980s a previously undescribed disease has affected moose in south-western Sweden. Investigations made to reveal evidence of a viral aetiology have proved unsuccessful. Trace element studies in apparently healthy moose shot during regular hunting suggested a trace element imbalance, with excessive molybdenum uptake causing secondary copper deficiency. The results also indicated a possible chromium deficiency. To verify this hypothesis, an experimental study was performed in male goats fed a semi-synthetic diet for 1.5 years. The animals were kept and treated in four groups: Controls, Cu-deficient group (group 1), Cr-deficient group (group 2), and combined Cu- and Cr-deficient group with additional supplementation of tetrathiomolybdate for 10 weeks at the end of the study (group 3). The present paper presents tissue contents of trace and minor elements, haematology and clinical chemical parameters. Feed consumption and weight development, as well as pathological and histopathological investigations, were also performed in this study, but these results are presented elsewhere. Changes in trace element concentrations were determined by comparing groups 1, 2 and 3 with the control group. Increased concentrations were observed for Al, Ca, Co, Fe, Mo, Pb, Se in the liver; for Al, Cd, Co, Cr, Mo in the kidneys; and for Mn and Mo in the ribs. Considerable accumulation of Mn in ribs seems to be a useful way to determine oxidative stress. Decreases in Mg and P in all organs and blood serum is characteristic of Cu deficiency and molybdenosis. Also the ratio of Ca/Mg was increased as the result of tissue lesions causing an intracellular increase in Ca and decrease in Mg. The trace element changes observed in group 1 were enhanced by the Mo supplementation in group 3,

resulting in characteristic patterns, 'spectra' of changes. The alterations were not as remarkable in group 2 as in the two other groups. However, Cr deficiency considerably influenced Al, Co, V and to a smaller extent also Mn in ribs. In groups 1 and 2, only a few minor changes were detected in the haematological parameters, probably caused by increased adrenal activity after transportation of the animals. In group 3, severe anaemia was present but also a leukopenia. For the different clinical chemical parameters measured, all three groups showed changes, explained mainly by the altered activity of enzymes induced by trace element deficiencies and imbalance. Impaired carbohydrate and lipid metabolism was seen in groups 1 and 3, with increased concentrations of glucose, lactate and triglycerides in serum. Increased concentrations of total bilirubin were measured in all three groups (bile stasis was also seen post mortem). A considerably increased concentration of serum urea was found in group 3, although there were no indications of renal insufficiency or dehydration. Regarding hormones, a substantial decrease was seen in thyroxine (T4) in group 3 as a result of the molybdenosis, but a minor decrease was also seen in group 1. Insulin on the other hand showed increased levels in group 3--and especially in group 2 due to the Cr deficiency but also affected by the molybdenosis. As could be expected, Cu deficiency (groups 1 and 3) caused low levels of caeruloplasmin, secondarily affecting the Fe metabolism in these animals. Protein abnormalities, detected as altered electrophoretic patterns of serum proteins, were also seen mainly in group 3. The findings were also confirmed by multivariate data analysis, where PCA revealed the overall impact of the deficiencies, and PLS regression coefficients indicated the influence on the various analytes.

Grand Forks Human Nutrition Research Center

Leslie M. Klevay M.D., S.D. in Hyg.

Recent Research Accomplishments

Clofibrate, a lipid-lowering drug, improves copper nutriture. Clofibrate will lessen the hypercholesterolemia of copper deficiency. The effect is mediated by an increase in liver copper. This observation led to the concept of cholesterotropic and cuprotropic chemicals. Some of these--for example, aspirin, clofibrate and sodium phytate--lower plasma cholesterol and enhance copper metabolism. Others--for example, ascorbic acid, cholesterol plus cholic acid and zinc--raise plasma cholesterol and inhibit copper metabolism. Extra dietary copper can abolish the hypercholesterolemia caused by feeding cholesterol plus cholic acid. Since 1924, cholesterol plus cholic acid have been fed to animals to induce atherosclerosis. This procedure induces copper deficiency in rats. Cholesterol fed to rabbits without cholic acid lowers liver copper and may induce copper deficiency. This method has been used since 1913 in the induction of atherosclerosis.

Hypercholesterolemia and impaired glucose tolerance have been induced in men by feeding a low copper diet. Prolonged ingestion of a diet containing 0.8 mg of copper per day produced reversible increases in plasma cholesterol and the height of the glucose tolerance curve. Hypercholesterolemia, glucose intolerance and diets this low in copper are common in the U.S. population.

Copper deficiency induces atrial thrombosis. For approximately 20 years, the adverse effects of certain diets on mice were attributed to the diets being high in fat. In reality, copper had been left out of the diets. Adequate copper prevented abnormal blood clotting and abnormal cardiograms and promoted far greater longevity. This finding is similar to that of an earlier experiment in which a diet high in cholesterol had little effect on mice if dietary copper was adequate. The clots accumulate because the ability to dissolve blood clots is impaired in copper deficiency.

Abnormal electrocardiograms and hypercholesterolemia may be more sensitive indices of copper deficiency than is anemia. Among nonanemic rats deficient in copper, abnormalities were found in the following (in order, beginning with greatest change): liver iron, heart dopamine, liver copper, plasma cholesterol, heart weight and heart norepinephrine. There is a close statistical relationship between liver copper and most of these measurements.

Copper deficiency produces abnormal cardiac anatomy. Mitochondrial membranes deteriorate in hearts of rats deficient in copper; debris and vacuoles are seen. The collagen fibers that hold the cardiac muscle cells together are poorly developed. The activity of choline phosphotransferase is decreased in copper deficiency; this change may partially explain some of the anatomical changes noted.

The original observation by Dr. Klevay (1973) linking copper metabolism and cholesterol metabolism has been confirmed in at least 20 independent laboratories. This paper is among the more frequently quoted from the American Journal of Clinical Nutrition, was the subject of a Citation Classic essay in Current Contents, and was the subject of a 20th anniversary editorial in Nutrition.

Adult rats deficient in copper are hypertensive. The decreased blood pressure of weanling rats made deficient in copper may be caused partly by decreased activity of angiotensin converting enzyme in plasma in addition to structural defects of heart and arteries.

A new way of explaining the clinical variability of specific human illnesses has been developed. Four classes of etiologic agents are known: toxicity, heredity, infection and deficiency. Illnesses that are caused by cooperating members of two classes have been identified--for example, nutritional deficiency induced by a toxic agent. Three- and four-way cooperations also exist; 15 cooperative mechanisms have been identified.

Kidneys of rats fed salt and deficient in copper fail with poor perfusion of blood and very large (greater than 90%)

decrease in aldosterone and plasma renin. Kidney failure was produced with half the salt in half the time in comparison to classical experiments.

Rats fed a diet deficient in copper were given either beer or water to drink because of extensive data demonstrating that modest consumption of beer is associated with less death from heart disease than is abstinence from alcoholic beverages. Beer-drinking rats live nearly six times as long with less heart damage and higher liver copper. Results were not from either the alcohol or the copper in beer; rather, animals absorbed and retained copper better.

Slight copper deficiency was induced in young pigs by feeding their mothers high doses of zinc during pregnancy; the normal conversion of cartilage into bone during development was retarded. They also had lower copper in heart and liver, had abnormal anatomy of the heart and had less of the "good cholesterol", HDL, in blood, otherwise they seemed normal.

Both copper deficiency and the psychological stress of intermittent, close confinement increases the blood pressure of adult rats. Rats low in copper with stress have the highest blood pressures. Copper deficiency increases sodium in hearts. Copper is an antioxidant nutrient because it is needed for an important enzyme that destroys superoxide, a harmful material produced by the body when it fights inflammation. Impaired defense against oxidation contributes to the increase in blood pressure, cholesterol and clotting found in copper deficiency. Abnormal utilization of salt by the deficient heart may explain some of the abnormal electrocardiograms found in copper deficiency.

Diets in the United States seem to be low in copper in comparison to putative requirements; 35% of daily diets probably contain less than 1.0 mg copper. Diets containing amounts of copper proved insufficient for volunteers in controlled experiments are readily available to the U.S. population. A unified theory is proposed that explains the high prevalence of ischemic heart disease in terms of dietary copper deficiency. Copper deficiency may induce this illness by weakening the connective tissue of arteries which are bathed in abnormal lipids and are under greater tension from high blood pressure. Arterial injury may be increased by decreased defense against oxidizing metabolites and by glycosylation of proteins. These changes result in abnormal cardiac physiology. Some of the benefits of diets enriched with nuts and soy protein in studies done elsewhere may be the result of these foods being high in copper. That is, they are dietary copper supplements. When dietary fat is decreased, dietary copper is increased because fat is nearly free of copper.

More than 70 similarities between animals deficient in copper and people with ischemic heart disease have been identified. The most important of these are glucose intolerance, hypercholesterolemia, abnormal electrocardiograms, hyperuricemia, hypertension, the differential susceptibility of males and females, and the impaired ability to dissolve blood clots. Female mice are more likely to die with excessive blood clots than are male mice; women with ischemic heart disease are more likely than men to die with excessive clots.

Protein Discovery Leads Researchers to New Suspect in Iron Anemia

From: <http://www.berkeley.edu/news/berkeleyan/1999/0224/protein.html>

By Kathy Scalise, Public Affairs
Posted February 24, 1999

If you're slugging down iron pills but remain weak and anemic, the culprit may not be iron at all, but another metal: copper. A new genetic find explaining why is described by a Berkeley scientist and his colleagues in this month's issue of the journal *Nature Genetics*.

The researchers discovered a protein, hephaestin, that appears critical for moving iron to the bloodstream. This protein contains copper and cannot be produced in the absence of copper. Thus in some cases, having too little copper present even with an ample iron supply might cause anemia, said the lead author on the paper, Assistant Professor Christopher Vulpe of the Division of Nutrition and Toxicology in the College of Natural Resources.

The new protein may also help explain what Vulpe describes as the number one inherited disease in Caucasians, hemochromatosis. It results from too much iron in the body and can cause diabetes if it kills insulin-producing cells in the pancreas, or "iron heart" if too much of the metal accumulates in that organ and causes cardiac arrest.

Vulpe's collaborators on the project included researchers from UC San Francisco, the University of Utah and the University of Queensland in Australia.

Hephaestin was isolated from mice and named after the Greek god for metal-working, Hephaestus. The protein is produced by the gene *Heph*, also discovered by the researchers and reported in the *Nature* paper, and is tethered to the membrane of intestinal cells. The researchers suspect it is a "multi-copper ferroxidase" protein that contains copper and works on iron molecules.

Vulpe led the original study while a postdoctoral fellow in the laboratory of Professor Jane Gitschier of UCSF. Gitschier said in a recent UCSF statement that "more work needs to be done to determine if and how often genetic defects in iron transport occur in humans."

In describing the possible role of the new protein, Vulpe traced the path of iron through the body.

Iron, he said, usually originates in the food supply, either as "heme," a cage of iron that transports oxygen in

blood and comes mainly from meats, or as "free" iron from other sources. Both kinds of iron are processed by the gut -- stomach and intestine -- where they are converted by means not well understood to a form of iron readily used by the body. Finally, the iron winds up in the intestinal epithelial cells, ready for export to red blood cells, muscle tissue and organs.

But somehow "it has to get out of the gut and into the bloodstream," said Vulpe.

This is particularly difficult, he said, because the so-called "hydrophobic" intestinal membrane wants to reject the charged iron molecule.

So hephaestin comes into play. Probably acting as a helper molecule forming a complex with a yet unknown transport protein, it allows iron to make its way through the membrane.

In fact, hephaestin may act like an "on/off" switch to control the flow of iron into the body, said Vulpe. Perhaps in the presence of hephaestin, more iron is pumped into the blood, and when hephaestin stops production, the pumping also soon halts.

While a certain amount of iron is vital for survival, about 10 percent of infants and women of childbearing age in the U.S. -- about 8.5 million people -- are iron deficient. Many other people suffer from having too much iron circulating in the body, a syndrome called hemochromatosis, which can also have toxic effects.

When the body functions correctly, excess iron remains trapped in the intestine and is harmlessly excreted. Disease results only after too much iron escapes from the intestine and into the blood.

The UC researchers plan to investigate whether hephaestin plays a role in hemochromatosis.

They suspect improper regulation of the Heph gene may result

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DEEPER STUDIES

When you start looking into hyperthyroidism, hypothyroidism, and thyroid cancer, you can look deeper, deeper, and deeper..... At some point we should find the mechanisms by which nutrients control thyroid function. Once we understand what is going on at the deeper chemical level, we will have a better idea of how the nutrients, that we can see affect thyroid function, actually affect thyroid metabolism.

As we start this deeper investigation, there are two things we'll look at first: the tyramines and monoamine oxidase (MAO) and monoamine oxidase inhibitors (MAOI). Click on the links to the left.

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DHEA

DHEA is a hormone called dehydro-epiandrosterone which is a precursor of testosterone in the body. DHEA is used by many people for increased energy and libido and by body builders and athletes for its muscle-building and sports performance enhancing effects. I was using DHEA when I developed hyperthyroidism and always felt that it was a causative factor. I stopped taking it when I started developing hyperthyroidism but this did not stop the progression of the hyperthyroidism. I have experimented with it since and am pretty convinced that not only does it promote hyperthyroidism but the effects last many months after usage is discontinued.

As I was researching phthalates (see [Phthalates](#) under Toxic Chemicals) which have been shown to have effects on the thyroid, including promoting hyperactivity of the thyroid (hyperthyroidism), I discovered that DHEA, like the phthalates, is a hypolipidemic (fat-lowering) agent. Thus there seems to be a known biological basis for concluding that the use of DHEA could lead to hyperthyroidism. I talked to a person in the nutritional supplement department of my health food store about DHEA usage and she told me that many of the companies that were producing DHEA supplements have discontinued them apparently because of the negative health effects that users have been experiencing. Among these effects are heart palpitations upon exercising and increased resting heart rate, which are exactly the same symptoms that hyperts experience. My conclusion is to avoid all use of DHEA and if you have been using it and have developed hyperthyroidism you should recover by discontinuing usage, following the supplement recommendations for hyperts, and increasing fat intake to compensate for the hypolipidemic effects. Be patient, since recovery may be slow due to the long-term effects of the DHEA.

Also note in the following study that the antipsychotic drugs,

Comp Biochem Physiol C Pharmacol Toxicol Endocrinol 1995 Jun;111(2):317-23

Hypolipidemic agents alter hepatic mitochondrial respiration in vitro.

Chance DS, McIntosh MK

Department of Food, Nutrition, and Food Service Management, University of North Carolina at Greensboro 27412, USA.

The direct effects of three different classes of structurally diverse hypolipidemic agents on respiration were studied in mitochondria isolated from donor Sprague-Dawley rats. Two classes of peroxisome proliferators (i.e. plasticizers and hypolipidemic hormones and drugs) and one class of peroxisome inhibitors (i.e. anti-psychotic drugs) were studied. The phthalate ester plasticizers dibutylphthalate, ethylhexanoic acid and di(2-ethylhexyl) adipate, the hypolipidemic hormones or drugs dehydro-epiandrosterone (DHEA), thyroxine (T4), triiodothyronine (T3), gemfibrozil, clofibrate and naphthoflavone, and the anti-psychotic drugs chlorpromazine, thioridazine and fluphenazine were studied. As the dose of the plasticizer dibutylphthalate increased from 8 to 200 $\mu\text{mol/l}$, there was a decrease ($P < 0.05$) in state 3 (+ADP) respiration and in the respiratory control ratio for both substrates tested. The anti-psychotic drug chlorpromazine decreased state 3 malate + pyruvate-supported respiration and increased state 3 succinate-supported respiration. As the concentration of all three anti-psychotic drugs increased, there was a linear increase in state 4 respiration (-ADP) and a decrease in the respiratory control ratio for both substrates tested. As the dose of the hypolipidemic agents DHEA, gemfibrozil and T4 increased, there was a linear reduction in state 3 malate + pyruvate-supported respiration. However, when succinate was used as the substrate to support respiration, only the thyroid hormones significantly decreased state 3 respiration. Gemfibrozil, T4 and T3 increased state 4 respiration, regardless of the substrate used. As the dose of clofibrate, gemfibrozil, and the thyroid hormones increased, there was a linear reduction in the respiratory control ratio for both substrates tested.

NOTE: To view the article with Web enhancements, go to:

<http://www.medscape.com/ASHP/AJHP/2000/v57.n22/ajhp5722.01.pepp/ajhp5722.01.pepp-01.html>

DHEA: Dehydroepiandrosterone

Joseph Pepping, Pharm.D.

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Introduction

Dehydroepiandrosterone (DHEA) and its active metabolite, DHEA sulfate (DHEAS), are endogenous hormones synthesized and excreted primarily by the zona reticularis of the adrenal cortex in response to adrenocorticotrophic hormone. The exact mechanism of action and clinical role, if any, of DHEA and DHEAS remain unclear. Epidemiological data indicate an inverse relationship between serum DHEA and DHEAS levels and the frequency of cancer, cardiovascular disease (in men only), Alzheimer's disease and other age-related disorders, immune function, and progression of HIV infection.^[1] Animal (primarily rodent) studies have suggested many beneficial effects of DHEA, including improved immune function and memory and prevention of atherosclerosis, cancer, diabetes, and obesity. Many of the benefits seen in animal studies have yet to be shown in humans.^[1-3]

Uses

Clinically substantiated (yet still controversial) uses of DHEA include replacement therapy in patients with low serum DHEA levels secondary to chronic disease, adrenal exhaustion, or corticosteroid therapy; treating systemic lupus erythematosus (SLE), improving bone density in postmenopausal women; improving symptoms of severe depression; improving depressed mood and fatigue in patients with HIV infection; and increasing the rate of reepithelialization in patients undergoing autologous skin grafting for burns.^[1,4-8] Other possible uses (with some supporting clinical studies) include enhancing the immune response and sense of well-being in the elderly, decreasing certain cardiovascular risk factors, and treating male erectile dysfunction.^[4,8-12] Use of DHEA to slow or reverse the aging process, improve cognitive function, promote weight loss, increase lean muscle mass, or slow the progression of Parkinson's disease and Alzheimer's disease is clinically unsubstantiated.^[3,4,9]

Pharmacology

In women, the synthesis of DHEA and DHEAS occurs almost exclusively in the adrenal cortex, whereas in men the testes secrete approximately 5% of DHEAS and 10-25% of DHEA.^[3] Minute amounts are synthesized de novo in the brain.^[3,13] In young adults the adrenal cortex secretes approximately 4 mg of DHEA and 25 mg of DHEAS per day.^[2] During gestation, large amounts of DHEA and DHEAS are secreted by the fetal adrenal glands. At birth, output drops to negligible amounts in both sexes and remains that way until five to seven years of age. At the onset of adrenarche, the adrenal glands gradually resume DHEA and DHEAS production, which accelerates through puberty. DHEA and DHEAS output is maximal between the ages of 20 and 30 years and then starts a decline of approximately 2% per year, leaving a residual of 10-20% of the peak production by the eighth or ninth decade of life.^[2,14-16]

DHEA and DHEAS are interconvertible by sulfohydrolases in peripheral and adrenal tissues.^[3] Some 64-74% of the DHEAS produced each day is converted to DHEA, but only 13% of the DHEA produced is metabolized to DHEAS.^[2,17,18] In humans, the brain-to-plasma ratios for DHEA and DHEAS are 4-6.5 and 8.5, respectively, indicating a neuroendocrine role for these hormones.^[2,19,20]

DHEA and DHEAS serve as the precursors of approximately 50% of androgens in men, 75% of active estrogens in premenopausal women, and 100% of active estrogens after menopause.^[2,16] There appears to be a sex-specific response to DHEA replacement therapy in humans. In postmenopausal women (ages 50-65), supraphysiological doses of 100 mg of DHEA per day have predominantly androgenic effects, increasing testosterone levels approximately 300% over baseline levels.^[21] In older men (mean \pm S.D. age, 58.8 \pm 5.1 years), 100 mg/day did not affect testosterone or dihydrotestosterone levels, but 17 beta-estradiol and estrone levels were increased over baseline by 37% and 225%, respectively ($p < 0.0001$ for both).^[22] It has been hypothesized that the increase in serum estrogens may provide a mechanism for beneficial cardiovascular effects in men; however, clinical studies addressing the possible cardioprotective effects of DHEA have been inconclusive.

Several mechanisms of action of DHEA and DHEAS other than their role as precursors of the sex hormones have been proposed. In the central nervous system, both DHEA and DHEAS appear to affect neurotransmitter receptors. In rodents, DHEAS binds to the γ -aminobutyric acid (GABA)/benzodiazepine-receptor complex (GABA-RC) and acts as a negative noncompetitive modulator of GABA-RC. DHEA, on the other hand, appears to have GABA-agonist effects on the GABA-RC. DHEA selectively enhances the neuronal response to N-methyl-D-aspartate.^[3,4] Also, DHEA and DHEAS appear to have neurotrophic effects, increasing the number of neurofilament-positive neurons and regulating the motility and growth of corticothalamic projections in cultured mouse embryo brain cells.^[23-25]

Supraphysiological oral doses of DHEA (100-300 mg/day) in humans have been found to inhibit the synthesis of thromboxane A₂ in activated platelets, reduce plasma plasminogen activator inhibitor type 1 and tissue plasminogen activator antigen, increase serum levels of insulin-like growth factor 1 (IGF-1), and increase cyclic guanosine monophosphate and nitric oxide synthesis (either directly or via increased levels of IGF-1).^[4,26-28] These effects suggest that DHEA may be beneficial in improving circulation in the microvasculature and regulating some of the risk factors of cardiovascular disease, such as platelet aggregation and ischemia. Clinical studies in this area have been equivocal, with a majority showing an inverse relationship between DHEA or DHEAS levels and cardiovascular morbidity and mortality in men but not in women.^[29] However, a recently published five-year epidemiologic cohort study found no statistically significant correlation between serum DHEA or DHEAS levels and the development of atherosclerosis in men or women.^[30]

DHEA may play a positive role in modulation of the immune response. Clinical studies in elderly persons have demonstrated that oral DHEA doses of 50 mg/day increase IGF-1 levels ($p < 0.01$) and cause functional activation of T cells (increases in CD8+ and CD56+ cells [natural killer cells] and enhanced cytotoxic activity).^[4,9,31,32] Serum levels of interleukin-6 (a proinflammatory cytokine involved in the pathogenesis of osteoporosis, rheumatoid arthritis, atherosclerosis, Alzheimer's disease, Parkinson's disease, and beta-cell malignancies) increase significantly with age and are inversely correlated with serum DHEA and DHEAS levels ($p < 0.001$). In addition, DHEA, DHEAS, and androstenedione inhibit the production of interleukin-6 by peripheral blood mononuclear cells in a concentration-dependent manner ($p < 0.001$).^[33]

Pharmacokinetics

Oral absorption of DHEA is excellent. The volume of distribution is 17.0-38.5 L for DHEA and 8.5-9.3 L for DHEAS. DHEA and DHEAS are converted into several active metabolites, including androstenedione, testosterone, estrone, estradiol, and estriol (Figure 1). The elimination half-life of DHEA is 15-38 minutes, whereas the half-life of DHEAS is 7-22 hours. Renal excretion accounts for 51-73% of the elimination of DHEAS and its metabolites.^[2,4,34-36]



Figure 1. Synthesis of dehydroepiandrosterone (DHEA), DHEA sulfate (DHEAS), and other steroids. The listing of more than one enzyme indicates a multistep process. aro = aromatase, DOC = deoxycorticosterone, HSD = hydrosteroid dehydrogenase, HSO = hydrosteroid oxidoreductase, HSS = hydrosteroid sulfatase, KSR = ketosteroid reductase, R = reductase, scc = side-chain cleavage, SH = sulfohydrolase, P-S = pregnenolone sulfate, THDOC = tetrahydrodeoxycorticosterone, THP = tetrahydroprogesterone. Reprinted from reference 3, with permission.

Clinical Studies

To date, clinical studies of DHEA in patients with specific diseases have yielded generally inconclusive results. Most of the studies were open label or had very small samples. Most of the studies discussed below were randomized, double-blind, placebo-controlled trials in which the oral dosage was 300 mg/day. Tummala and Svec^[37] demonstrated that incremental increases in serum DHEA and DHEAS levels appear to plateau at an oral DHEA dosage of 300 mg/day and inferred that doses greater than this have little additional therapeutic value.

Postmenopausal Bone Density

In a randomized, double-blind, placebo-controlled study by Baulieu et al.,^[10] 280 healthy men and women ages 60-79 years were given DHEA 50 mg/day orally for 12 months. Increases in bone mineral density ($p < 0.05$) and decreases in biochemical markers of bone turnover ($p < 0.01$ for serum C-terminal peptide and $p < 0.05$ for serum bone alkaline phosphatase) were observed at 12 months in women older than 70 but not in any other subgroup.

Systemic Lupus Erythematosus

DHEA supplementation has shown promise for the treatment of SLE. In a randomized, double-blind trial,^[38,39 28] women with SLE received DHEA 200 mg/day for three months. In the DHEA group, the SLE Disease Activity Index score and both the patients' and the physicians' overall assessments of disease activity decreased, whereas small increases were seen in the placebo group. However, significance was achieved only for the visual-analogue-scale component of the index ($p = 0.022$). Lupus flares occurred less frequently in the treatment group than in the placebo group (three versus eight flares, $p = 0.053$), and a nonsignificant decrease in prednisone requirements was noted in the treatment group (from a mean \pm S.D. daily dose of 12.4 ± 3.2 mg to 9.1 ± 2.3 mg, compared with an increase from 5.3 ± 1.37 mg to 7.3 ± 2.9 mg in the placebo group). Serum titers of antibodies to double-stranded

DNA and levels of complement components C3 and C4 did not change significantly between the groups.

Well-being and Cognition

In a randomized, placebo-controlled, crossover trial, 30 patients ages 40-70 years were given 50 mg of DHEA orally daily.⁹ Within two weeks, this dose restored serum DHEA levels in both men and women to those found in young adults. With DHEA treatment, 67% of the men and 84% of the women perceived an increase in physical and psychological well-being. However, the study has been criticized for its use of an open-ended questionnaire for self-assessment of well-being.^[40]

At present, there are no rigorous data to support an improvement in memory or other aspects of cognitive function after DHEA replacement therapy. Low endogenous levels of DHEA and DHEAS do not appear to be associated with an increased risk of dementia.^[41]

Depression

The possible relationship between depression and serum DHEA and DHEAS levels is intriguing; however, more research is needed. Some authors have suggested that abnormal diurnal variations in serum DHEA and DHEAS levels, as well as abnormally high cortisol- to-DHEA ratios, may be causative factors in depression in adults and depression with comorbid panic or phobic disorders in adolescents.^[3,42-44]

In a randomized, double-blind trial by Wolkowitz et al.,^[45] 22 patients who had major depression (a Hamilton Rating Scale for Depression [HAM-D] score of 16 or greater) and who were either medication free or stabilized on antidepressant regimens received DHEA (30 mg/day for weeks 1 and 2, 60 mg/day for weeks 3 and 4, and 90 mg/day for weeks 5 and 6) or placebo. At the end of the six weeks, the mean decrease in the HAM-D score was 30.5% in the treatment group and 5.3% in the placebo group ($p < 0.04$). Five of 11 patients in the treatment group were considered responders (at least a 50% decrease in HAM-D score), compared with none of the 11 patients in the placebo group.

Effects in HIV-Infected Patients

In a recent open-label trial evaluating the effect of DHEA on depressed mood and fatigue, 45 HIV-positive patients (39 men and 6 women) received oral DHEA doses of 200-500 mg/day for eight weeks.^[11] Of the 32 patients who completed the trial, 23 (72%) had an improvement in mood and 26 (81%) had a reduction in fatigue. There was a significant increase in body cell mass and libido but no effect on CD4+ lymphocyte counts or testosterone levels in men. The positive effects on mood, fatigue, and body cell mass continued for an additional four weeks in a subsequent double-blind phase of the study. Christeff et al.^[46] have noted an inverse relationship between serum DHEA and DHEAS levels and the immunologic deterioration in HIV patients, which suggests a role for DHEA and other androgens in the normal functioning of the immune system.

Effects on Physical Variables

A randomized, double-blind, placebo-controlled crossover trial by Morales et al.^[21] looked at the effects of oral DHEA 100 mg/day in 16 subjects 50-65 years of age. Baseline levels of serum DHEA, DHEAS, androstenedione, testosterone, and dihydrotestosterone were at or below the low end of the range for young adults. In both sexes, DHEA 100 mg/day restored serum DHEAS to levels at or slightly above the upper limit of the young-adult range. In women, androstenedione, testosterone, and dihydrotestosterone were increased to three to five times baseline levels ($p < 0.001$ for each hormone), or to levels above the sex-specific ranges for young adults, whereas in men only androstenedione was significantly increased above baseline ($p < 0.05$). Serum IGF-1 levels increased by a mean \pm S.D. of $16\% \pm 6\%$ ($p = 0.04$) in men and $31\% \pm 12\%$ in women ($p = 0.02$). In men but not women, fat body mass decreased by $6.1\% \pm 2.6\%$ ($p = 0.02$), and there were increases in knee muscle strength ($15.0\% \pm 3.3\%$, $p = 0.02$) and lumbar back strength ($13.9\% \pm 5.4\%$, $p = 0.01$). No changes in basal metabolic rate, bone mineral density, urinary pyridinoline cross-links, fasting insulin, glucose, cortisol, or lipids were observed in either sex.

Dosage

Physiological replacement dosages of oral DHEA in healthy people older than 40 years are in the range of 20-50 mg/day for men and 10-30 mg/day for women.^[2,4,8] These dosages are usually adequate to increase serum DHEAS to the levels found in adults 20-30 years of age and to bestow the reported benefits of a heightened sense of well-being in both sexes, increased bone mineral density in postmenopausal women, and amelioration of erectile dysfunction in men. Higher dosages may be necessary for increasing suppressed DHEA and DHEAS levels

secondary to chronic disease, adrenal exhaustion, and corticosteroid therapy. Replacement doses of DHEA are usually taken once daily in the morning.

It is imperative that serum DHEAS concentration be measured before DHEA replacement therapy is started. The serum DHEAS level should be checked at least annually to ensure that it is in the normal range. To minimize adverse effects and maximize benefits, it is suggested that replacement dosages in healthy adults be adjusted to maintain serum levels of DHEAS in the second or third quartile of sex-specific, young-adult ranges.

Pharmacologic dosages of 200 mg/day have been successfully used in patients with SLE. Dosages of 200-500 mg/day have been used in HIV-positive patients with depressed mood and fatigue. It is not known what effect long-term physiological or supraphysiological doses of DHEA may have on suppression of the zona reticularis of the adrenal cortex; however, there does not appear to be feedback inhibition of DHEA or DHEAS secretion by the hypothalamic-pituitary axis.^[2]

Adverse Effects

Increased facial sebum production, acneiform dermatitis, and mild hirsutism have been reported in women taking DHEA in physiological or supraphysiological dosages (25-200 mg/ day).^[4,21,38] Hepatitis was reported in a postmenopausal woman with preexisting high titers of antinuclear antibodies who received a single oral dose of 150 mg of DHEA; causality could not be established.^[4,47] A supraphysiological dosage of DHEA (100 mg/day) was shown to increase androstenedione, testosterone, and dihydrotestosterone levels threefold to fivefold in postmenopausal women.^[21] The long-term effects of these increases in androgen levels in women are not known. A nested case-control study by Dorgan et al.^[48] found that postmenopausal women (not taking DHEA or hormone replacement therapy) whose levels of endogenous DHEAS were in the highest quartile had a significantly higher risk of breast cancer (risk ratio, 2.8 [95% confidence interval 1.1-7.4]) than women whose levels of endogenous DHEAS were in the lowest quartile.

Drug Interactions

Calcium-channel blockers and metformin increase levels of endogenous DHEAS, whereas corticosteroids and insulin significantly decrease them.^[3] Supraphysiological dosages of DHEA can increase serum triazolam levels because of an inhibition of metabolism.^[8] Theoretically, aromatase inhibitors, such as chrysin (5,7-dihydroxyflavone), an extract from the plant *Passiflora coerulea*, can increase levels of androgens, including DHEA and DHEAS, in both men and women. Kroboth et al.^[3] published an excellent review of the effects of disease, diet, exercise, and medications on endogenous DHEA and DHEAS levels.

Contraindications

DHEA supplementation is contraindicated in patients with a history of sex hormone-responsive cancers, such as breast, ovarian, endometrial, and prostate cancer. Women with a family history of postmenopausal, estrogen-sensitive cancers and men with benign prostatic hypertrophy or a family history of prostate cancer should carefully weigh the risks and benefits of DHEA replacement therapy with their physician. If replacement therapy is deemed necessary, close monitoring of serum DHEAS and its androgenic and estrogenic metabolites should be performed frequently. DHEA supplementation should be avoided during pregnancy and lactation.

Conclusion

Clinical data suggest that DHEA may have a role in hormone replacement therapy in patients with low endogenous DHEA and DHEAS levels due to chronic diseases, adrenal exhaustion, corticosteroid therapy, and advancing age. However, as a potent steroid precursor, DHEA can significantly increase androgen levels in women and may enhance the progression of estrogen and testosterone-sensitive cancers. Supplementation with DHEA should never be undertaken without direct medical supervision. The long-term effects of DHEA supplementation are unknown.

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DIABETES

There seem to be certain connections linking diabetes with thyroid disease. I'm pretty certain that most cases of diabetes are the result of nutrient deficiencies. If you look on this page there is a study (Title: High-dose biotin, an inducer of glucokinase expression, may synergize with chromium picolinate to enable a definitive nutritional therapy for type II diabetes) showing that biotin and chromium picolinate work very well together to control diabetes. What is interesting about this is that we've seen that biotin is very important for copper metabolism and is often deficient in hyperT. Further down on this page there is a study showing that copper levels are high in diabetics. Generally when copper levels are high it means that copper is not being used properly because of other deficiencies. Copper is essential for the production of insulin, so it's possible that the lack of other nutrients which work with copper are preventing copper from being used to produce insulin, and therefore an insulin deficiency (diabetes) results. Possibly this is where biotin and chromium fit in.

Another interesting possible connection between diabetes and hyperT is that experimenters have found that diabetes can be controlled by administering tungsten. A quote from one study: "Results of uncontrolled trials on volunteers accumulated in Japan also suggest that tungstate effectively regulates diabetes mellitus without detectable side effects." There are other bits of information about tungsten and a possible connection between tungsten and copper which leads me to suspect that a tungsten deficiency is involved in hyperT also. Tungsten seems to be extremely difficult to get from foods and is unavailable as a supplement. The only sources I've found are the trace mineral supplements that list tungsten (over 1 mg per liter), and water from the eastern Sierra Nevada mountains (like Crystal Geyser--a brand found here in California).

Another hint that tungsten is involved in diabetes is that tungsten seems to play a role in the retina, perhaps for the detection of light (tungsten makes a good filament for light bulbs) and diabetics can get retinopathy.

Besides possible deficiencies of biotin, chromium, and tungsten, it's possible that diabetes could also result from a copper deficiency, since copper is necessary for insulin production. It may be that many diabetics have high copper, but some have low.

Med Hypotheses 1999 May;52(5):401-6

High-dose biotin, an inducer of glucokinase expression, may synergize with chromium picolinate to enable a definitive nutritional therapy for type II diabetes.

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Glucokinase (GK), expressed in hepatocyte and pancreatic beta cells, has a central regulatory role in glucose metabolism. Efficient GK activity is required for normal glucose-stimulated insulin secretion, postprandial hepatic glucose uptake, and the appropriate suppression of hepatic glucose output and gluconeogenesis by elevated plasma glucose. Hepatic GK activity is subnormal in diabetes, and GK may also be decreased in the beta cells of type II diabetics. In supraphysiological concentrations, biotin promotes the transcription and translation of the GK gene in hepatocytes; this effect appears to be mediated by activation of soluble guanylate cyclase. More recent evidence indicates that biotin likewise increases GK activity in islet cells. On the other hand, high-dose biotin suppresses hepatocyte transcription of phosphoenolpyruvate carboxykinase, the rate-limiting enzyme for gluconeogenesis. Administration of high-dose biotin has improved glycemic control in several diabetic animals models, and a recent Japanese clinical study concludes that biotin (3 mg t.i.d. orally) can substantially lower fasting glucose in type II diabetics, without side-effects. The recently demonstrated utility of chromium picolinate in type II diabetes appears to reflect improved peripheral insulin sensitivity--a parameter which is unlikely to be directly influenced by biotin. Thus, the joint administration of supranutritional doses of biotin and chromium picolinate is likely to combat insulin resistance, improve beta-cell function, enhance postprandial glucose uptake by both liver and skeletal muscle, and inhibit excessive hepatic glucose production. Conceivably, this safe, convenient, nutritional regimen will constitute a definitive therapy for many type II diabetics, and may likewise be useful in the prevention and management of gestational diabetes. Biotin should also aid glycemic control in type I patients.

Thyroid disease and diabetes

A DGReview of :["Practical Pointers: Thyroid Disease and Diabetes"](#)
Clinical Diabetes

02/22/2000

By Mark Greener

Thyroid disease is widespread and prevalence increases with advancing age. However, as assessing thyroid function is reliable and inexpensive, certain high-risk groups - such as neonates, the elderly and diabetics - should undergo regular screening, a recent review notes.

Thyroid dysfunctions complicate diabetes management and the diagnosis of diabetes complications, the paper adds. For example, 6.6 per cent of the general population suffers from thyroid dysfunction, compared to between 10.8 and 13.4 per cent of people with diabetes. It is easy to understand the high prevalence of thyroid disease in women with type 1 diabetes - they are at greater risk because of their diabetes and because thyroid disease is more prevalent in women. In addition, postpartum thyroiditis is three times more common among women with diabetes than the non-diabetic population.

Clinically, thyroid dysfunction may undermine diabetes control. For example, hyperthyroidism may worsen glycaemic control and increase insulin requirements. Indeed, thyrotoxicosis may unmask subclinical diabetes. The author points to three issues which arise from this:

- Hyperglycaemia may improve during thyrotoxicosis treatment.
- Unexplained worsening hyperglycaemia may be due to hyperthyroidism.
- Hyperthyroidism may lead to poor glycaemic control.

While hypothyroidism markedly alters carbohydrate metabolism, such changes are rarely clinically significant. However, as less insulin is degraded, the exogenous insulin requirement may be lower. Moreover, hypothyroidism often produces dyslipidaemias, including elevated triglyceride and low-density lipoprotein (LDL) cholesterol concentrations. Therefore, hypothyroidism can exacerbate coexisting dyslipidaemias in type 2 diabetes. Thyroxine reverses these lipid abnormalities.

Postpartum transient thyroid dysfunction is common. As glucose control may fluctuate, the author stresses the importance of monitoring thyroid function - approximately 30 per cent of women do not recover and require thyroxine replacement.

The author notes that diagnosing thyroid dysfunction can be difficult. For example, poor glycaemic control produces symptoms similar to hyperthyroidism, such as weight loss despite increased appetite as well as fatigue. Clinicians need to be careful not to confuse severe diabetic nephropathy and hypothyroidism: both produce oedema, fatigue, pallor and weight gains. Finally, poorly controlled diabetes may alter thyroid function.

Against this background, the serum TSH immunoassay offers the most reliable and sensitive screening test for thyroid dysfunction. However, screening for anti-thyroid peroxidase (TPO) antibodies in people with type 1 diabetes may predict autoimmune thyroid disorders.

Management is generally similar to that in the non-diabetic population. However, the author warns that L-thyroxine therapy may exacerbate angina by increasing myocardial contractility and heart rate. She adds that clinicians should consider treating subclinical hypothyroidism if patients either have elevated serum LDL cholesterol exacerbated by hypothyroidism or detectable serum anti-TPO antibodies.

The author concludes that thyroid dysfunction is common among diabetic patients and can produce metabolic disturbances. Therefore, regularly screening diabetic patients allows early treatment. Type 1 patients expressing anti-TPO antibodies should be screened annually. In anti-TPO negative patients, a TSH assay every two to three years suffices. Among patients suffering from type 2 diabetes, clinicians should consider a TSH at diagnosis and then at least every five years.

Pediatrician 1983-85;12(4):213-9

The role of trace elements in juvenile diabetes mellitus.

Tuvemo T, Gebre-Medhin M.

There is accumulating evidence that the metabolism of several trace elements is altered in insulin-dependent diabetes mellitus and that these nutrients might have specific roles in the pathogenesis and progress of this disease. Magnesium deficiency is the most evident disturbance of metal metabolism in diabetes mellitus. Hypomagnesemia might increase the risk of ischemic heart disease and severe retinopathy. Increased urinary loss of zinc is a commonly encountered feature of diabetes. High-dose oral zinc might enhance wound healing, although data regarding diabetes are lacking. Chromium increases tissue sensitivity to insulin and tends to raise high-density lipoprotein (HDL) cholesterol and the HDL:low-density lipoprotein ratio. Selenium is involved in processes which protect the cell against oxidative damage by peroxides produced from lipid metabolism. There is one report of elevated serum selenium in diabetic children although the clinical significance of this finding is still unclear. An insulin-like effect has recently been attributed to vanadium in experimental animals, a finding of potential interest to man. Current knowledge does not implicate iron, iodine, manganese, cobalt, nickel, silicone, fluoride, molybdenum or tin in the pathophysiology of diabetes. Appropriate trace element supplementation might prove beneficial in ameliorating some physiological deficiencies associated with diabetes and prevent or retard secondary complications. However, properly designed and well-documented trials, especially on magnesium supplementation, need to be performed before rationales for such supplementation are developed. The potential roles of vanadium, chromium and selenium in diabetes constitute challenging areas for further experimental and clinical research.

Diabetes Res Clin Pract 1990 Aug-Sep;10(1):59-63

Early increase in histamine concentration in the islets of Langerhans isolated from rats made diabetic with streptozotocin.

Azevedo MS, Silva IJ, Raposo JF, Neto IF, Falcao JG, Manso CF

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Sprague-Dawley rats were separated in 4 groups. G1 received streptozotocin (ST). G2 received nicotinamide (NC) followed by ST. G3 was a NC control and G4 was a citrate control. The rats were sacrificed after 28 h and the islets isolated. Histamine and histaminase were determined. In the islets there was an increase in histamine content in G1 and a smaller increase in G2. The first two groups differ significantly and also in relation to the control groups. A decrease in islet histaminase does not seem responsible for the increased histamine, since group 2 (NC + ST) which had no diabetes, had a lower activity than group 1 (ST). It is suggested that histamine liberation by ST may be related to the diabetogenic effect of this drug.

PMID: 1701117, UI: 91065188

REGULAR PHYSICAL ACTIVITY HALVES DIABETES RISK IN POSTMENOPAUSAL WOMEN

Postmenopausal women who engage in any physical activity on a regular basis

are approximately half as likely to develop type 2 diabetes as those who

rarely or never exercise, according to study results published in the January issue of the American Journal of Public Health.
<http://diabetes.medscape.com/15503.rhtml>

WESTPORT, Mar 30 (Reuters Health) - Despite concerns that thiazide diuretics and beta-blockers may promote the development of type 2 diabetes mellitus, the results of a new study indicate that only beta-blockers are associated with an increased risk.

The findings appear in the March 30th issue of the New England Journal of Medicine. One of the study's authors told Reuters Health, "We want to sound a yellow alert about beta-blockers," but the risk of diabetes should nevertheless be weighed against the proven cardiovascular benefits of beta-blockers.

Dr. Frederick L. Brancati, of Johns Hopkins School of Medicine in Baltimore, said that the findings should alleviate concerns about most antihypertensive medications, including diuretics. He and his and colleagues with the Atherosclerosis Risk in Communities Study, analyzed data on 12,550 nondiabetic subjects age 45 to 64 years. Examination at baseline included blood-pressure measurement and assessment of medications.

At 3 and 6 years, participants were screened for diabetes based on fasting serum glucose concentrations.

Overall, patients with hypertension were 2.5 times more likely than nonhypertensives to develop type 2 diabetes mellitus, the researchers report. After adjustment for potential confounders, patients taking a thiazide diuretic, angiotensin-converting-enzyme (ACE) inhibitor or calcium-channel antagonist did not have a greater risk of developing diabetes than those not taking any antihypertensive medications. But the relative hazard for diabetes mellitus was 1.28 among patients taking a beta-blocker.

Based on the results, "concern about increasing the risk of diabetes should not discourage physicians from prescribing thiazide diuretics for the treatment of hypertension in adults," the authors write. They also note while beta-blockers do appear to raise the risk of diabetes, "but this adverse effect must be weighed against the proven benefits of beta-blockers in reducing the risk of cardiovascular events."

In an editorial accompanying the study, Dr. James R. Sowers, of the State University of New York Health Science Center at Brooklyn, and Dr. George L. Bakris, of Rush-Presbyterian-St. Luke's Medical Center in Chicago, Illinois, call for prospective studies to determine whether using ACE inhibitors along with beta-blockers might counteract the increased risk of diabetes.

"Until such studies are conducted, beta-blockers will continue to have an important therapeutic role in patients with hypertension who have known coronary artery disease and in hypertensive patients who have diabetes, a population in which the prevalence of underlying coronary disease is high," they conclude.
N Engl J Med 2000;342:905-912,969-970.

Title

Alterations of antioxidant tissue defense enzymes and related metabolic parameters in streptozotocin-diabetic

rats--effects of iodine treatment.

Author

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Source

Wien Klin Wochenschr, 104(14):409-13 1992

Abstract

This study reports on the effect of streptozotocin (STZ) induced diabetes on water soluble-SH and -SS, as well as on hepatic glutathione peroxidase (GSH-Px), catalase and superoxide dismutase (**SOD**) activity and on malondialdehyde (MDA) content. In addition, we determined serum concentrations of glucose, cholesterol, triglycerides and thyroxine, and thyroid weight. To elucidate the possible impact of exogenous iodine on impaired free radical tissue defense mechanisms STZ-diabetic rats were exposed to iodine brine providing for a daily iodide uptake of about 300 micrograms/kg body weight. STZ-exposure caused a decline in thyroid weight (p less than 0.01) and in total serum thyroxine (p less than 0.001), as well as a fall in hepatic catalase (CAT) activity (p less than 0.01) versus control group. Impairment of catalase activity was related to serum glucose level ($r = -0.569$, p less than 0.01), while hepatic MDA was positively related to serum glucose ($r = +0.5$, p less than 0.01). No protective effects of iodine brine were seen with regard to impairment by STZ of antioxidant enzyme status. We conclude that impairment by STZ of antioxidant enzymes may contribute to STZ-dependent experimental diabetes.

WESTPORT, Mar 22 (Reuters Health) - Regardless of dietary patterns, African-American children have an increased risk of type 2 diabetes compared with white children, according to a report in the March issue of the *American Journal of Clinical Nutrition*.

Dr. Michael I. Goran and colleagues at the University of Southern California in Los Angeles, California, evaluated the diets of 54 white children and 41 African-American children based on three 24-hour recalls. They also measured total cholesterol, triacylglycerol, insulin sensitivity and acute insulin response.

Cholesterol levels were not significantly different between the groups, the researchers report, and triacylglycerol levels were significantly lower among African Americans. However, acute insulin response was increased among African Americans, and insulin sensitivity was lower.

"Intake of fruit and vegetables was significantly higher, and dairy intake lower, in African Americans than in white children after adjustment for social class and total energy intake," Dr. Goran's team found. "However, neither macronutrient nor food group intake accounted for the ethnic differences in triacylglycerol and acute insulin response."

The investigators did find several associations between diet and insulin. According to the report, "carbohydrates and fruit intakes were positively associated with insulin sensitivity...and vegetable intake was negatively associated with acute insulin response."

In an editorial in the same journal, Dr. Sidika E. Kasim-Karakas, from the University of California at Davis writes, "Although [these researchers suggest] that dietary factors are not responsible for the insulin resistance in African Americans, it also shows that a high vegetable intake may have a favorable effect on insulin sensitivity. Further understanding of the mechanisms of the ethnic differences in insulin resistance will be important to reducing the morbidity and mortality related to diabetes mellitus and coronary artery disease."

Am J Clin Nutr 2000;71:725-732.

VEGAN DIET HELPS CONTROL DIABETES

WESTPORT, Sep 13 (Reuters Health) - A low-fat, vegetarian diet can help improve glycemic control in patients with type diabetes, and reduce the need for oral hypoglycemic medication even in the absence of exercise or controlled energy consumption.

In addition, patients who adhere to the vegan diet lose more weight than those consuming a conventional low-fat diet for 12 weeks, Dr. Andrew S. Nicholson, of the Physicians Committee for Responsible Medicine in Washington, DC, and colleagues report in the August issue of *Preventive Medicine*.

The investigators randomized 12 patients with noninsulin-dependent diabetes mellitus to one of the two diets for 12 weeks.

During the study, fasting serum glucose dropped an average of 28% in patients on the low-fat vegan diet and 12% in those randomized to the conventional low-fat diet. Mean weight loss was 7.2 kg in the vegan group and 3.8 kg in the conventional group, according to the report.

One of six patients in the vegan group completely discontinued oral hypoglycemic medication during the study while three patients were able to reduce their dosage of these agents. By comparison, "[n]o patients in the control group reduced medication use," the investigators point out.

High-density lipoprotein (HDL) cholesterol levels declined in both groups during the study, more so in vegan patients, but this change did not appear "...to be associated with elevated atherosclerotic risk in the context of a low total serum cholesterol concentration."

Although the findings appear promising, the study was small and the authors warn that the results require confirmation through further research.

Prev Med 1999;29:87-91.

Title

Preliminary observation on the metabolism in spontaneous hereditary diabetic Chinese hamster (Shanyi colony).

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Source

Chin Med J (Engl), 110(9):711-4 1997 Sep

Abstract

OBJECTIVE: To observe the changes of tissue *lithium* content and its relationship with glucose metabolism

in spontaneous hereditary diabetic Chinese hamsters (SHDCH). METHODS: Twenty diabetic and ten normal Chinese hamsters were paired and separated randomly into four groups: controls (C), diabetics (D), controls treated with *lithium* carbonate (CT) and diabetics treated with *lithium* carbonate (DT). The *lithium* carbonate treatment was administered with drinking water containing *lithium* carbonate (0.2 mg/ml). Blood glucose levels were determined at 0, 1, 3, 5, 6th month, and insulin levels at 1, 3, 6th month. The *lithium* contents in liver, kidney and muscles were determined at the end of 6th month, using wet digestion assay and ICP-AES. Concentrations of fructosamine, lactic acid, GPT, BUN were also evaluated. RESULTS: The data showed that in Group D the *lithium* levels in hepatic tissue were lower than in Group C ($P < 0.05$), and *lithium* contents in kidney and muscle also decreased. In Group DT, the *lithium* contents in tissues were higher than in Group D ($P < 0.05$) and similar to Group C. Blood glucose levels and fructosamine concentrations decreased while insulin and lactic acid levels did not alter significantly. GPT and BUN levels did not change in both Group CT and Group DT. CONCLUSIONS: There is *lithium* deficiency in hepatic, renal and muscular tissues from diabetic Chinese hamsters. Low-dose and six-month-treatments of *lithium* carbonate can improve tissue *lithium* deficiency and glucose metabolism, and do not damage liver and kidney functions.

Growth Hormone Therapy May Accelerate Onset of Type 2 Diabetes in Predisposed Children

WESTPORT, Feb 18 (Reuters Health) - Children with glucose disorders who are treated with growth hormone (GH) develop type 2 diabetes at a rate six times that of children not treated with GH, researchers report in the February 19th issue of *The Lancet*.

Using the Pharmacia and Upjohn International Growth Study database, Dr. Wayne S. Cutfield, of the University of Auckland in New Zealand, and a multinational team determined that 43 of 23,333 children treated with growth hormone had confirmed glucose disorders, including 11 children with type 1 diabetes and 18 with type 2. Most children who developed diabetes were in puberty and had received GH for several years.

Among the children with type 1 diabetes, the incidence of disease and age at diagnosis did not differ from expected values, Dr. Cutfield's group reports. But among type 2 diabetics, disease incidence "was 34.4 cases per 100,000 years of GH treatment, which was sixfold higher than the incidence in children not treated with GH."

Discontinuation of GH therapy did not resolve type 2 diabetes. This "excludes a transient drug-induced effect such as that seen with high-dose glucocorticoid treatment," the authors note.

Dr. Cutfield and colleagues conclude that "GH therapy may...have hastened the onset of type 2 diabetes that would have occurred in adult life without GH therapy."

The authors recommend "that each child's glucose status be determined before starting GH therapy by measurement of hemoglobin A1c and fasting plasma glucose and insulin concentration." In addition, they say, "follow-up of patients is important for children with disorders at high risk of type 2 diabetes mellitus, such as obesity, Turner's syndrome, intrauterine growth retardation, Prader-Willi syndrome, and GH deficiency secondary to other causes."

In an editorial, Dr. William Jeffcoate of City Hospital in Nottingham, UK, says that the findings add weight to the case that widespread use of GH is not justified.

"In view of the possibility of a link between serum insulin-like growth factor-1 and carcinoma of the breast, prostate, and colon, the possibility of an adverse effect of GH on lipoprotein(a)1, the relation between fasting serum GH (within the normal range) and mortality in the Paris prospective study, and, now, the chance that some patients treated with GH might develop diabetes, the sceptical minority have a case," Dr. Jeffcoate says.

Lancet 2000;355:589-590,610-613.

Title

Vanadate, molybdate and *tungstate* for orthomolecular medicine.

Author

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Source

Med Hypotheses, 43(3):177-82 1994 Sep

Abstract

Recent studies indicate that oxyanions, such as vanadate (V) or vanadyl (IV), cause insulin-like effects on rats by stimulating the insulin receptor tyrosine kinase. *Tungstate* (VI) and molybdate (VI) show the same effects on rat adipocytes and hepatocytes. Results of uncontrolled trials on volunteers accumulated in Japan also suggest that *tungstate* effectively regulates diabetes mellitus without detectable side effects. Since these oxyanions naturally exist in organisms, oxyanion therapy, the oral administration of vanadate, vanadyl, molybdate, or *tungstate*, can be considered to be orthomolecular medicine. Therefore, these oxyanions may provide a viable alternative to chemotherapy. Many diseases in addition to diabetes mellitus might also be treated since the implication of these results is that tyrosine kinases are involved in a variety of diseases.

Title

Insulin-like actions of tungstate in diabetic rats. Normalization of hepatic glucose metabolism.

Author

Barber`a A; Rodr'iguez-Gil JE; Guinovart JJ

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Source

J Biol Chem, 269(31):20047-53 1994 Aug 5

Abstract

Oral administration of tungstate for 15 days normalized glycemia in streptozotocin-induced diabetic rats. Simultaneously, the alterations in hepatic glucose metabolism due to diabetes were almost completely counteracted by this treatment. Thus, 6-phosphofructo-2-kinase, L-pyruvate kinase, and glycogen phosphorylase alpha activities reached levels similar to those observed in healthy animals. Hepatic levels of fructose 2,6-bisphosphate and glycogen also recovered. However, the recovery of glucokinase activity and hepatic levels of glucose 6-phosphate was only partial. The total activity of glycogen synthase increased, although the activation state was not recovered. Moreover, mRNA levels of hepatic glucokinase, glycogen phosphorylase, and phosphoenolpyruvate carboxykinase were also normalized. Tungstate administration in healthy animals also affected all these parameters, although to a much lesser extent. All these effects were similar to those previously reported for vanadate, suggesting a common mechanism of action in vivo.

The following study indicates that while zinc and magnesium levels in diabetics are normal, copper levels are high. This may mean that iron levels are low, and this would be great additional information to determine what is deficient that is making copper levels high.

Postgrad Med J 1998 Nov;74(877):665-8

Copper, zinc, and magnesium levels in non-insulin dependent diabetes mellitus.

Zargar AH, Shah NA, Masoodi SR, Laway BA, Dar FA, Khan AR, Sofi FA, Wani AI

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A relationship has been reported between trace elements and diabetes mellitus. This study evaluated the role of such a relationship in 83 patients with non-insulin dependent diabetes mellitus (40 men and 43 women), with a mean duration of diabetes of 3.9 +/- 3.6 years. Patients with nephropathy were excluded. Thirty healthy non-diabetic subjects were studied for comparative analysis. Subjects were subdivided into obese and non-obese. Diabetic subjects were also subdivided into controlled and uncontrolled groups; control was based on fasting blood glucose and serum fructosamine levels. Plasma copper, zinc and magnesium levels were analysed using a GBC 902 double beam atomic absorption spectrophotometer. **Plasma zinc and magnesium levels were comparable between diabetic and non-diabetic subjects, while copper levels were significantly elevated ($p < 0.01$) in diabetic patients.** Age, sex, duration and control of diabetes did not influence copper, zinc, or magnesium concentrations. We conclude that zinc and magnesium levels are not altered in diabetes mellitus, but the increased copper levels found in diabetics in our study may merit further investigation of the relationship between copper and non-insulin dependent diabetes mellitus.

PMID: 10197198, UI: 99212947

Cow's Milk May Increase Child's Risk Of Type 1 Diabetes

June 14, 2000

NEW YORK (Reuters Health) - Consuming large quantities of cow's milk during childhood may increase the risk of developing type 1 diabetes in children who are already genetically susceptible to the disorder, results of a study suggest.

The team of Finnish researchers found that children who had a sibling with diabetes were more than five times as likely to develop the autoimmune disorder if they drank more than half a liter (about three glasses) of cow's milk a day, compared with children who drank less milk.

The study findings, published in the June issue of *Diabetes*, add to an ongoing debate over the role of cow's milk in the onset of type 1 diabetes.

"Our study is the first prospective study to suggest that cow's milk consumption during childhood is related to development of clinical diabetes in siblings of children with diabetes," lead author Dr. Suvi M. Virtanen with the University of Tampere, Finland, told Reuters Health.

However, more studies are needed to assess the possible interaction between genetic disease susceptibility and dietary exposures in the development of the disease, Virtanen added.

While it is not clear which component of cow's milk may increase risk of diabetes, researchers suspect that one of several proteins may be to blame, Virtanen explained. Similarly, it is not known how cow's milk increases the risk of type 1 diabetes, although Virtanen suspects that it may "program the immune system in a direction favoring an immune attack against insulin producing cells."

Type 1 diabetes is usually diagnosed in children or in adults younger than 30. The disorder is caused by an abnormal immune reaction that destroys the cells of the pancreas that produce insulin, the hormone that regulates blood sugar. People with type 1 diabetes usually take life-long insulin injections to regulate their blood sugar.

The investigators looked at children who consumed cow's milk in the first year of life and followed up when children were age 3 to 19. Some children had a sibling with type 1 diabetes and were examined for a genetic predisposition to the disorder.

Results show that children who developed diabetes were more likely to have consumed at least three glasses of milk daily before entering the study. The number of diabetics and nondiabetics who had breast-fed for at least 2 months or had received some cow's milk before 2 months of age did not differ, researchers found.

A greater number of children who developed diabetes were genetically susceptible to the disease. Seventy-nine percent of these children carried a particular genetic variation associated with diabetes while only 30% of those who did not develop diabetes were found to have this variation.

SOURCE: *Diabetes* 2000;49:912-917.

Niacin May Be Alternative to Statins for Diabetics With Peripheral Arterial Disease

WESTPORT, Sep 13 (Reuters Health) - Patients with type 2 diabetes who receive lipid-modifying doses of niacin show a significant increase in high-density lipoprotein cholesterol and a significant decrease in triglycerides and low-density lipoprotein cholesterol levels, according to results from the Arterial Disease Multiple Intervention Trial.

Dr. Marshall B. Elam, of the University of Tennessee, Memphis, and a multicenter team studied 468 patients with peripheral arterial disease, of whom 125 were diabetic. The team randomized all patients to receive either niacin, 3000 mg/day or the maximum tolerated dose, or placebo. Sixty-four diabetic patients received niacin, as did 173 nondiabetics. The trial ran for 60 weeks, which included a 12-week run-in period.

"Niacin use significantly increased HDL cholesterol by 29% and 29% and decreased triglycerides by 23% and 28% and LDL cholesterol by 8% and 9%, respectively, in participants with and without diabetes," the research team reports in the September 13th issue of *The Journal of the American Medical Association*.

In the subjects receiving placebo, Dr. Elam and colleagues detected "increases of 0% and 2% in HDL cholesterol and increases of 7% and 0% in triglycerides, and increases of 1% and 1% in LDL cholesterol." They also noted that glucose levels increased by 8.7 mg/dL in diabetics receiving niacin and by 6.3 mg/dL in the nondiabetics receiving niacin. All changes were statistically significant.

Additionally, Dr. Elam's group saw "no significant differences in niacin discontinuation, niacin dosage, or hypoglycemic therapy in participants with diabetes assigned to niacin versus placebo."

"Despite current recommendations against use of niacin in diabetes, the present study demonstrates that lipid-modifying doses of immediate-release niacin can be used safely in patients with stable, controlled, type 2 diabetes mellitus," Dr. Elam and associates conclude.

Moreover, they add, "niacin therapy may be considered as an alternative to statin drugs or fibrates in patients with diabetes in whom these agents are not tolerated, or in whom they fail to sufficiently correct hypertriglyceridemia or

low HDL cholesterol."

JAMA 2000;284:1263-1270.

The following article about cinnamon combined with the anecdotal stories of cinnamon cravings in persons with thyroid disease makes me wonder if there is something more in cinnamon than mentioned here. Perhaps cinnamon accumulates some nutrient that is important in correcting thyroid imbalance.

Cinnamon May Help Control Blood Sugar

Cinnamon may significantly help people with type 2 diabetes improve their ability to regulate their blood sugar. As a matter of fact, this study found that it increased glucose metabolism 20-fold.

- In a test tube and in animal studies, the spice appeared to increase glucose metabolism by about 20 times.
- Clinical trials using a cinnamon extract on humans are due to begin in 6 months.
- Researchers maintain that this could be a good means of lowering or controlling blood glucose levels at very little cost and could prove helpful to millions of people.
- Approximately 16 million Americans suffer from diabetes with 95% of them having type 2 diabetes, where the body's cells fail to recognize insulin.
- As a result, the amount of sugar in the blood remains high, leading to fatigue, blurred vision, and other problems. Over the long term, excess blood glucose can increase the risk of heart disease, kidney failure and blindness.
- Diabetes is the seventh-leading cause of death in the US, according to the American Diabetes Association. Yet, because of its influence in raising the risk of other problems, particularly heart disease, diabetes may be responsible for many more deaths than is attributed to it.

Dr. Richard A. Anderson, lead scientist at the Beltsville, Maryland-based Human Nutrition Research Center, a branch of the US Department of Agriculture (USDA), explained that his mostly unpublished research shows that a compound in cinnamon called methylhydroxy chalcone polymer (MHCP) makes fat cells more responsive to insulin by activating an enzyme that causes insulin to bind to cells and inhibiting the enzyme that blocks this process.

While it is too soon to recommend the spice as a regular treatment for type 2 diabetes, Dr. Anderson said patients could try adding 1/4 - 1 teaspoon of cinnamon to their food. "The worst that will happen is it won't do any good and the best is that it will help dramatically," he stated.

Preliminary Findings Announced by the USDA August, 2000.

The following study offers evidence that cadmium may be a factor in diabetes. If this is true then persons with diabetes may need to restrict intake of green leafy vegetables and other high cadmium foods.

Cigarette Smoking May Increase Risk of Diabetes

WESTPORT, CT (Reuters Health) Nov 29 - The results of a prospective study of more than 21,000 physicians indicate that smoking is associated with a substantial increase in the incidence of type II diabetes mellitus, researchers report in the November issue of the *American Journal of Medicine*.

"Smoking increases blood glucose levels after an oral glucose challenge and may impair insulin sensitivity," Dr. JoAnn E. Manson, of Brigham and Women's Hospital, Boston, and colleagues point out, which is one of the reasons why there may be a causal association between smoking and diabetes.

To investigate, the researchers examined the relationship between smoking and type II diabetes in a prospective cohort study of 21,068 US male physicians between the ages of 40 and 84 years. At the time of enrollment in 1982, none of the subjects had a diagnosis of diabetes mellitus, cardiovascular disease or cancer.

After an average of 12 years follow-up, 770 cases of type II diabetes mellitus were identified. Compared with those who had never smoked, smokers of 20 or more cigarettes daily had a 2.1 relative risk of diabetes. For fewer than 20 cigarettes daily, the corresponding figure was 1.4. For past smokers, the relative risk was 1.2.

After adjusting for factors such as body mass index and physical activity, the relative risks were 1.7 for smokers of 20 or more cigarettes daily, 1.5 for smokers of fewer than 20 cigarettes daily, and 1.1 for past smokers, compared with those who had never smoked. Total pack-years of smoking were also associated with increased risk.

The researchers conclude that "smoking is an independent and modifiable determinant of type II diabetes mellitus." Populations at high risk of the condition, they add, "should be considered for special targeted smoking interventions."

Am J Med 2000;109:538-542.

Sci Total Environ 2000 Apr 17;249(1-3):123-31

A syndrome of molybdenosis, copper deficiency, and type 2 diabetes in the moose population of south-west Sweden.

Frank A, Sell DR, Danielsson R, Fogarty JF, Monnier VM

Department of Clinical Chemistry, Faculty of Veterinary Medicine, Swedish University of Agricultural Sciences, Uppsala. dr.a.frank@rocketmail.com

Since the mid-1980s, a 'mysterious' disease has been afflicting the moose (*Alces alces* L.) population of south-western Sweden. Molybdenosis combined with secondary copper deficiency syndrome has been suggested as the cause of the clinical signs and of necropsy findings, supported by trace element analysis. Copper deficiency has long been associated with disturbed carbohydrate metabolism and also with oxidative stress. When testing the oxidative stress hypothesis, we found increased concentrations of the glycoxidation products pentosidine and carboxymethyl-lysine (CML), both in plasma proteins and in renal tissue, when compared with control values. The concentration of glycated lysine (furosine), a marker of hyperglycaemia, was also increased. These data, together with elevated insulin levels in affected moose, strongly suggest that they are suffering from an environmentally-induced, non-insulin-dependent type 2 diabetes.

Tungstate Improves Glucose Homeostasis in Diabetic Rats

WESTPORT, CT (Reuters Health) Feb 13 - Administration of sodium tungstate markedly reduces glycemia in a rat model of type 2 diabetes, Spanish researchers report in the January issue of *Diabetes*.

Dr. Joan J. Guinovart from Universitat de Barcelona and colleagues have previously shown that tungstate lowers blood glucose levels in rats made insulin deficient to simulate type 1 diabetes. In the current study, the researchers administered tungstate orally to 7.5-week-old Zucker diabetic fatty rats, which are "considered the closest available rat model to human type 2 diabetes associated with obesity."

The animals had begun to show hyperglycemia, and the treatment temporarily reversed this for about 10 days. Glucose levels then rose again but stabilized at about 200 mg/dL at day 24. In contrast, the glucose level of untreated rats rose to a maximum value of 450 mg/dL.

Tungstate treatment caused serum triglyceride levels to fall by 42%, and normalized hepatic concentrations of glucose-6-phosphate. The researchers also found that the treatment led to 55% higher glycogen levels in the liver compared with untreated diabetic or healthy rats. Treatment did not cause a significant change in phosphotyrosine-modified proteins in cultured hepatocytes from diabetic animals.

"These data suggest that tungstate administration to Zucker diabetic fatty rats causes a considerable reduction of glycemia, mainly through a partial restoration of hepatic glucose metabolism and a decrease in lipotoxicity," Dr. Guinovart and colleagues conclude.

Vitamin E Shows Promise In Treating Diabetes

June 5, 2001

WASHINGTON (Hearst Newspapers) - Break out that jar of wheat germ in the back of the refrigerator because it might help save your life if you are diabetic.

Scientists are assessing research that suggests high dosages of Vitamin E - naturally found in wheat germ, vegetable oils, margarine, whole-grain breads, nuts and peanut butter - may help stave off the ravages of diabetes.

The complications from diabetes can be devastating, including heart disease, eye and nerve damage, leading to amputations and kidney failure.

About 16 million Americans have the disease, which is caused by a deficiency of insulin, a hormone secreted by the pancreas and that is essential for converting sugar, starches and other foods into energy for cells. Lacking insulin, sugars build up in the blood rather than entering cells to fuel them. The result is that the body's cells literally can starve to death, causing the complications.

At the same time, the unprocessed sugar damages the weakened cell walls.

Some 798,000 new cases of diabetes are diagnosed annually in the United States. It is a chronic disease that has no cure and is the seventh leading cause of death in the United States, according to the Centers for Disease Control and Prevention in Atlanta.

Diabetes has two major subsets. In Type 1 diabetes, most often occurring in children and young adults, the body does not produce insulin and patients must take daily insulin injections to live. Type 1 accounts for about 10 percent of all diabetes cases.

In Type 2 diabetes, the body either doesn't make enough insulin or doesn't properly use it to convert foods. This is the most common form of the disease, comprising about 90 percent of all cases. Weight loss and exercise can control many of these cases.

African-Americans, Hispanic-Americans, American Indians and some Asian Americans and Pacific Islanders are at particularly high risk for Type 2 diabetes. Scientists believe high doses of Vitamin E help diabetics on at least two levels.

First, the vitamin acts as an antioxidant, a kind of chemical shield that protects cells against free radicals - potentially damaging byproducts of the body's metabolism. The U.S. National Institutes of Health in Bethesda, Md., says that free radicals can cause cell damage that may contribute to heart disease and certain cancers. And diabetics have an abnormally large supply of free radicals triggered by the high level of sugars, or glucose, in the blood.

Second, Vitamin E appears to arrest the effects of glucose. Dr. George King, professor of medicine at Harvard Medical School and research director of the Joslin Diabetes Center in Boston, explained that high glucose levels stimulate the development of an enzyme - known as PKC - that is particularly dangerous to diabetics.

"For some reason that isn't clear yet, Vitamin E in high doses not only is an antioxidant but it also inhibits the enzyme PKC. When that is done, you reverse or stop or prevent many of the blood-vessel complications we find in diabetes," said King, one of the country's leading Vitamin E researchers.

Damage to nerves, eyes, kidneys and heart appears to be slowed or arrested in diabetics when they take large daily doses of the vitamin, somewhere in the range of 1,000 international units or more. The typical over-the-counter supplement is around 250 to 400 IUs.

Vitamin E "could have dramatic consequences if a larger clinical trial showed that this can be helpful," King added.

Most of the studies showing a benefit have been conducted on small numbers of diabetics, usually under 200 patients. King said large pharmaceutical companies are reluctant to foot the bill for an expensive study with thousands of participants because no single company has a patent on the vitamin.

Likewise, the NIH tends to give vitamin studies low priority "because it's not as sexy as other medical developments," King lamented.

Some of the strongest recent evidence for a benefit to diabetics comes from researchers at the University of Texas Southwestern Medical Center in Dallas, where scientists found that Vitamin E reduced the risk of heart failure in diabetics. Heart disease is one of the most serious side effects of diabetes.

Researchers showed that Vitamin E curtailed the inflammation in blood vessels of the heart. Left unchecked, the swelling of the vessels can lead to heart disease. Researchers studied 75 patients who had Type 2 diabetes. Test subjects received 1,200 IUs of Vitamin E daily, and all of the participants experienced a drop-off in inflammation. Dr. Sridevi Devaraj, assistant professor of pathology and a lead researcher on the study, said the results were very encouraging.

"The study showed that Vitamin E significantly decreases micro-vascular complications" in diabetics, he said.

The American Diabetes Association says that some physicians prescribe Vitamin E supplements with a potency of up to 800 IUs per day for diabetes.

Anne Daly, a Springfield, Ill.-based dietitian and spokeswoman for the ADA, says that the vitamin "is pretty low risk and a possible benefit. But it's not a substitute for medicines people might be using (such as insulin injections or other sugar-lowering drugs). It's an adjunct."

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Role of Estrogen in Thyroid Disease

Estrogen plays a key role in my theory of thyroid disease. However, I don't see estrogen as a cause of thyroid disease. I see estrogen as an accelerator of the nutritional imbalances that underlie thyroid disease. Let me explain.

First, however, let me add that estrogen is not one hormone, but three: estradiol, estrone, and estriol. Most studies on estrogen use estradiol, which has the most biological function. I use the term estrogen so you'll know what I'm talking about, but the term estradiol is more accurate.

One of the most fascinating studies that I've run across was performed studying cadmium toxicity in rats. I believe that cadmium is principle player in the etiology of thyroid disease, but again, not the real cause.

While being female is the largest risk factor for developing thyroid disease, the second largest risk factor that has been identified, especially for hyperthyroidism, is smoking tobacco.

While many chemicals present in tobacco smoke have been identified which affect thyroid function, I believe that the most important ingredient of tobacco smoke which affects the thyroid is the heavy metal cadmium.

Cadmium is one of the most potent and long-lasting toxic metals known. Cadmium has been shown to kill animals at a concentration lower than any other commonly occurring toxic metal. Cadmium has been demonstrated to damage thyroid cells and this damage can be viewed in in vitro studies of thyroid cells in a culture.

Now to get back to our experimental studies of cadmium toxicity in rats. In this study, both female and male rats were castrated, thereby eliminating the bulk of production of the sex hormones, estrogen and testosterone. In this way estrogen and testosterone administered and the observed effects can be attributed to the administered hormones.

Both the castrated male and castrated female rats were given cadmium labeled with radioactive cadmium. Half of the cadmium administered rats were injected with estrogen and half with testosterone. The course of the cadmium in the body was then able to be followed because it was radioactively labeled.

The amazing result was that estrogen caused the cadmium to be incorporated into and retained by the body, while testosterone caused the cadmium to be excreted from the body. This is extremely significant and to me represents the key to understanding why 90% of the people with thyroid disease are female.

I've been thinking for a long time about this result. For a while I thought that females and males had different mechanisms for dealing with toxic metals. In males, testosterone protected the body by causing the rapid excretion of toxic metals into the blood stream and out of the body via urine and the bile system. In females, however, this strategy could have disastrous results because the female might be pregnant. If the toxic metals were put into circulation to be excreted, they would travel in the blood to the fetus and cause the fetus to be possibly damaged.

Now, however, I've come up with a different hypothesis, one that I like much better. What estrogen might be doing is causing the female body to absorb and store trace elements. This could be very valuable because the female needs to have a good store of these scarce trace elements in order to pass along a good amount to the offspring. A baby probably needs a good store of essential trace elements to protect it for years from running out. Also, because females lose significant amounts of blood each month during menstruation, and thereby lose essential trace elements like iron and copper, having a hormone like estrogen which increases the accumulation of trace elements would be very advantageous.

How could estrogen act as an accelerator of mineral accumulation in the body? Perhaps estrogen triggers the production of proteins which bind and store minerals in the body. There is a protein called metallothionein which performs this function in the body. Perhaps estrogen stimulates the body to manufacture more of this or a similar protein.

When I first started studying the effects of the hormones, estrogen and its antagonist, progesterone, on thyroid function it appeared that estrogen caused the body to slow thyroid function like copper does and progesterone caused the body to increase thyroid function, like zinc.

However, this theory was challenged more than once by women who reported that taking supplemental estrogen caused their hyperthyroidism to worsen. I tried to ignore these observations because they didn't fit into this theory. Now however, these observations make sense.

If estrogen is an accelerator of mineral uptake into the body, it can have opposite effects. Zinc accelerates thyroidal function and copper slows it down. When copper gets deficient, the thyroid produces excessive hormone and hyperthyroidism results. The balance of zinc and copper is important in maintaining normal thyroid function and the proper ratio seems to be about 5:1 for females and 10:1 or higher for males.

If the diet has a zinc/copper ratio which is too high, which is pretty much characteristic of some diets,

estrogen can have an accelerative effect of causing this zn/cu imbalance in the body to get too high and causing hyperthyroidism. If the zinc/copper ratio is too low, then estrogen can have the opposite effect, of causing the body to incorporate too much copper and not enough zinc and thereby slowing the thyroid too much. This may be the most prevalent situation since there are more people with hypothyroidism than hyperthyroidism.

The important thing about estrogen is that it probably does not affect the thyroid itself, but only has thyroidal effects because it influences mineral uptake. Taking estrogen will not cause the correction of thyroid disease but can facilitate correction if the proper minerals in the proper ratios are taken.

Thinking of estrogen as an accelerator of body accumulation of minerals, both essential and toxic, can also shed light on the controversial results seen from consuming foods with estrogen-like substances like tofu. Many reports indicate that tofu promotes hypothyroidism while others report that it promotes hyperthyroidism. If tofu is eaten with a diet high in cadmium, such as from eating large amounts of green leafy vegetables or from smoking, then the estrogen-like substances could accelerate the body's uptake of cadmium, leading to hyperthyroidism or TED. However, if tofu is consumed along with a diet high in beans and nuts (high in copper), the copper intake could be accelerated and hypothyroidism could result. Tofu is also high in phytates which bind zinc, increasing the possibility of hypothyroidism.

Also, estrogen probably increases the retention of all minerals. Another observation is that females suffer from the effects of mercury toxicity from silver amalgam dental fillings at a much higher rate than males. This is probably another effect of estrogen acting as an accelerator of mercury uptake into the body.

Mercury is one of the metals that cause hypothyroidism since it is a direct antagonist to selenium. Selenium deficiency is known to cause hypothyroidism and goiter and selenium is the trace element that is essential to form the deiodinase enzymes which convert T4 (the hormone our thyroid gland makes) into T3 (the hormone our cells use).

Since many people have mercury dental fillings, those people with high estrogen (women in child-bearing years or supplementing with estrogen) will more likely suffer from hypothyroidism as a result of mercury toxicity from dental fillings.

File:

ESTROGEN

This first study shows that estrogen can be diminished by cadmium, but progesterone is not.

Title

Cadmium interferes with steroid biosynthesis in rat granulosa and luteal cells in vitro.

Author

Paksy K; Varga B; L'az'ar P

Address

National Institute of Occupational Health, Budapest, Hungary.

Source

Biometals, 5(4):245-50 1992 Winter

Abstract

Recently, cadmium has been described to disturb ovarian function in rats. In this paper the direct influence of cadmium on steroid production of ovarian cells in vitro has been studied. Granulosa and luteal cells were obtained from proestrous and pregnant rats, and incubated with 0, 5, 10, 20 or 40 micrograms ml⁻¹ CdCl₂ in the presence or absence of 0.1-1000 ng ml⁻¹ follicle stimulating hormone (FSH) or luteinizing hormone (LH) for 24 or 48 h. Production of progesterone (P) and 17 beta-estradiol (E2) by granulosa and that of P by luteal cells were measured by radioimmunoassay. In FSH-stimulated granulosa cell cultures, 5 and 40 micrograms ml⁻¹ CdCl₂ suppressed P accumulation to 65 and 10%, respectively; accumulation of E2 (at 5 micrograms ml⁻¹ CdCl₂) decreased to 44%. P production of LH-supported luteal cells dropped to 86 and 66%, respectively, when 5 and 40 micrograms ml⁻¹ CdCl₂ was added to the medium. **No alteration in basal P accumulation occurred in granulosa and luteal cell cultures following incubations with 20 and 40 micrograms ml⁻¹ CdCl₂, whereas basal E2 production of granulosa cells was markedly diminished.** It is concluded that CdCl₂ suppressing steroid synthesis in vitro exerts a direct influence on granulosa and luteal cell function.

The following study shows that estradiol is low in Wilson's disease patients. My theory for this is that there is a metabolic problem with copper metabolism either from a genetic error or a deficiency of a nutrient needed for copper metabolism. This results in copper not being able to fulfill all of its functions. Since copper seems necessary to form the enzymes which convert progesterone to estradiol, there is a resulting deficiency of estradiol.

Title

Endocrine studies of the ovulatory disturbances in Wilson's disease (hepatolenticular degeneration).

Author

Kaushansky A; Frydman M; Kaufman H; Homburg R

Source

Fertil Steril, 47(2):270-3 1987 Feb

Abstract

Women with Wilson's disease may have severe oligomenorrhea or amenorrhea whose cause is unknown. The endocrine profile of four such cases was investigated by measuring basal values and the response to dynamic tests of hypothalamic, pituitary, thyroid, and adrenal function, which all proved normal. Ovarian function was disturbed, as witnessed by low estradiol, high total testosterone (T) levels with normal free T, and mildly elevated androstenedione. An interference of ovarian follicular aromatase activity possibly due to copper intoxication could explain these findings as the cause of the ovulatory disturbances of Wilson's disease.

Estrogen is degraded by estrogen sulfotransferase (EST) (a selenium enzyme) which is regulated by the levels of progesterone.

Title

Regulation of estrogen *sulfotransferase* in human endometrial adenocarcinoma cells by progesterone.

Author

Falany JL; Falany CN

Address

Department of Pharmacology and Toxicology, University of Alabama, Birmingham, Alabama 35294, USA.

Source

Endocrinology, 137(4):1395-401 1996 Apr

Abstract

During the secretory phase of the human menstrual cycle, the endometrium is minimally responsive to the estrogens secreted from the ovaries. Conjugation of beta-estradiol (E2) with sulfate is thought to be an important mechanism in the regulation of the levels of active E2 in endometrial tissue. Estrogen sulfation is reportedly increased during the secretory phase in response to the high levels of progesterone secreted by the ovaries. Estrogen sulfotransferase (hEST), a distinct form of human cytosolic sulfotransferase (ST) with an affinity for E2 and estrone at low nanomolar concentrations, has recently been cloned and expressed in mammalian cells and in bacteria (J Steroid Biochem Mol Biol 52:529, 1995). At least two other forms of human cytosolic ST, dehydroepiandrosterone ST (hDHEA-ST) and the phenol-sulfating form of phenol-ST (hP-PST), also conjugate estrogens but at micromolar concentrations. This report describes the specific induction of hEST in human Ishikawa endometrial adenocarcinoma cells by progesterone as a model for the increases in estrogen sulfation observed in women during the secretory phase of the menstrual cycle. Treatment of Ishikawa cells with 10 microns progesterone for 48 h resulted in a 7-fold increase in the sulfation of 20 nM E2. The sulfation of selective substrates for human dehydroepiandrosterone sulfotransferase (hDHEA-ST) and the two forms of phenol sulfotransferase (hP-PST, hM-PST) were not affected by treatment with progesterone. The levels of immunoreactive hEST and hEST mRNA in the Ishikawa cells were both increased by progesterone, whereas the levels of immunoreactive hDHEA-ST, hP-PST, and hM-PST were not altered. hEST activity was not induced by treatment of Ishikawa cells with varying concentrations of E2, testosterone, or cortisol. The induction of hEST by progesterone was inhibited by RU-486, indicating that progesterone is acting via the progesterone receptor. These results indicate that progesterone is capable of specifically inducing hEST and estrogen sulfation in human Ishikawa adenocarcinoma cells and suggest a mechanism for increasing estrogen sulfation in the endometrium during the secretory phase of the menstrual cycle.

The following article describes the prevalence of estrogen mimics. Of particular interest is the statement that the estrogen mimic "bisphenol-A was found to contaminate the contents of canned foods." This may explain why cat hyperthyroidism occurs at a much higher rate among cats fed canned food and may be a direct suggestion that persons with thyroid disease should avoid eating any food from cans. The estrogen mimics may have very powerful effects on increasing the uptake of cadmium. Also note that "Bisphenol-A is also used in dental sealants and composites."

1 : J Steroid Biochem Mol Biol 1998 Apr;65(1-6):143-50

An updated review of environmental estrogen and androgen mimics and antagonists.

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For the last 40 y, substantial evidence has surfaced on the hormone-like effects of environmental chemicals such as pesticides and industrial chemicals in wildlife and humans. The endocrine and reproductive effects of these chemicals are believed to be due to their ability to: (1) mimic the effect of endogenous hormones, (2) antagonize the effect of endogenous hormones, (3) disrupt the synthesis and metabolism of endogenous hormones, and (4) disrupt the synthesis and metabolism of hormone receptors. The discovery of hormone-like activity of these chemicals occurred long after they were released into the environment. Aviation crop dusters handling DDT were found to have reduced sperm counts, and workers at a plant producing the insecticide kepone were reported to have lost their libido, became impotent and had low sperm counts. Subsequently, experiments conducted in lab animals demonstrated unambiguously the estrogenic activity of these pesticides. Man-made compounds used in the manufacture of plastics were accidentally found to be estrogenic because they fouled experiments conducted in laboratories studying natural estrogens. For example, polystyrene tubes released nonylphenol, and polycarbonate flasks released bisphenol-A. Alkylphenols are used in the synthesis of detergents (alkylphenol polyethoxylates) and as antioxidants. These detergents are not estrogenic; however, upon degradation during sewage treatment they may release estrogenic alkylphenols. The surfactant nonoxynol is used as intravaginal spermicide and condom lubricant. When administered to lab animals it is metabolized to free nonylphenol. **Bisphenol-A was found to contaminate the contents of canned foods; these tin cans are lined with lacquers such as polycarbonate. Bisphenol-A is also used in dental sealants and composites. We found that this estrogen leaches from the treated teeth into saliva; up to 950 microg of bisphenol-A were retrieved from saliva collected during the first hour after polymerization.** Other xenoestrogens recently identified among chemicals used in large volumes are the plasticizers benzylbutylphthalate, dibutylphthalate, the antioxidant butylhydroxyanisole, the rubber additive p-phenylphenol and the disinfectant o-phenylphenol. These compounds act cumulatively. In fact, feminized male fish were found near sewage outlets in several rivers in the U.K.; a mixture of chemicals including alkyl phenols resulting from degradation of detergents during sewage treatment seemed to be the causal agent. Estrogen mimics are just a class of endocrine disruptors. Recent studies identified antiandrogenic activity in environmental chemicals such as vinclozolin, a fungicide, and DDE, and insecticide. Moreover, a single chemical may produce neurotoxic, estrogenic and antiandrogenic effects. It has been hypothesized that endocrine disruptors may play a role in the decrease in the quantity and quality of human semen during the last 50 y, as well as in the increased incidence of testicular cancer and cryptorchidism in males and breast cancer incidence in both females and males in the industrialized world. To explore this hypothesis it is necessary to identify putative causal agents by the systematic screening of environmental chemicals and chemicals present in human foods to assess their ability to disrupt the endocrine system. In addition, it will be necessary to develop methods to measure cumulative exposure to (a) estrogen mimics, (b) antiandrogens, and (c) other disruptors.

The following information may support the idea that estrogen is an accelerator of cadmium uptake into the body since cadmium is probably the heavy metal that induces lung cancer. The fact that lung cancer typically strikes women in their 60s may stem from the post-menopausal decline of estrogen which decreases the uptake of zinc (or possibly copper) which may protect the lungs from cadmium-induced damage. Because of the very long half-life of cadmium, it stays in the body much longer than zinc or copper.

High estrogen linked to lung cancer

From Science News, Vol. 157, April 22, 2000.

Women seem more susceptible than men to the carcinogenic effects of tobacco smoke, research has indicated. New findings suggest that estrogen may also play a role.

When estrogen is present, some cells produce a protein on their surfaces called an estrogen receptor. The hormone can then bind to these cells and spur cell proliferation. Pharmacologist Jill M. Siegfried of the University of Pittsburgh found evidence of estrogen receptors in a five kinds of tumors from patients with non-small-cell lung cancer, the most common variety of lung cancer. Healthy lung cells rarely show estrogen receptors.

Initial tests showed that the tumors made the RNA that directs production of the estrogen receptor known as alpha. A second experiment revealed a profusion of estrogen receptor alpha on the surface of tumor cells, she says.

In another experiment, which compared lung tumors from two men and two women, Siegfried found that the surfaces of cancerous cells from the women had roughly twice as many estrogen receptor alpha molecules as those from the men had.

Women have more estrogen circulating in their systems before menopause than after it. Yet, on average, lung cancers strike women in their early 60s. It may take years for the carcinogenic effect of estrogen to result in diagnosable cancer, she says.

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FLUORINE

Rough file:

Nutrition Almanac, pg. 100: "Aluminum is easily absorbed by the body and is accumulated in the arteries. Highest concentrations are found in the lungs, liver, thyroid, and brain." "Average amounts in the diet do not interfere with the absorption or utilization of calcium, phosphorus, zinc, copper, selenium, iron, or magnesium. Flouride may be interfered with, but more tests must be made."

Nutrition Almanac, pg. 133 (Selenium): "Overdoses (of selenium) can interfere with flouride assimilation, which helps prevent tooth decay. Children who live in areas where the soil is rich in selenium show signs of increased decayed, missing and filled teeth."

The Doctors' Vitamin and Mineral Encyclopedia: "The major source of flouride is from drinking water. In the United States, the typical daily intake of flouride from drinking water is from 1-2 milligrams and from foods, 0.2 to 0.6 milligrams. Foods high in flouride include seafood, animal meat (especially if the bones are included in the preparation), and tea. One cup of tea can have from 1-4 milligrams of flouride. Foods poor in flouride include fruits, cereals, milk and other dairy products."

Eur J Clin Pharmacol 1979 Sep;16(3):211-5

Influence of milk products on fluoride bioavailability in man.

Ekstrand J, Ehrnebo M

The effect of milk products on the gastrointestinal absorption of fluoride from sodium fluoride tablets was studied in five healthy subjects. Two different diets were tested: (1) 250 ml standardized milk (3% fat) and (2) 500 ml of milk, 3 pieces of white bread with cheese and 150 ml of yoghurt. The 100% bioavailability of sodium fluoride tablets during fasting was greatly decreased by coadministration of milk products: with Diet 1 the absolute bioavailability calculated from combined plasma and urine data was in the range 50--79% and with Diet 2 it ranged from 50--71%. It is suggested that the decreased bioavailability produced by dairy products should be taken into account when establishing fluoride dosage regimens for prophylaxis of caries.

PMID: 499322, UI: 80046881

Biochem Biophys Res Commun 1986 Sep 30;139(3):932-9

Identification of an enzymatic activity that hydrolyzes protein-bound ADP-ribose in skeletal muscle.

Chang YC, Soman G, Graves DJ

An enzymatic activity present in high-speed supernatant fluids of rat skeletal muscle was found that catalyzes the release of ADP-ribose from ADP-ribosylated-modified lysozyme. The nature of the product was proved by chromatographic studies and proton nuclear magnetic resonance spectroscopy. The enzyme activity is stimulated by Mg²⁺, dithioerythritol, and fluoride. These results and those published earlier (Soman, G., Mickelson, J.R., Louis, C.F., and Graves, D.J. (1984) *Biochem. Biophys. Res. Commun.* 120, 973-980) show that ADP-ribosylation is a reversible process in skeletal muscle.

PMID: 3768008, UI: 87025860

Fluoride: Hidden Danger in Your Drinking Water and Toothpaste

This common additive to your water supply, and ingredient in the toothpaste you and your children use may be contributing to the increased rates of hypothyroidism -- and other health concerns -- in the U.S. . . without improving dental health

What is Fluoride?

Fluoride is an element from the halogen group, as are iodide and chloride. It is commonly added to the water supply as hydrofluosilicic acid, silicofluoride or sodium fluoride. Fluoride is also found as an additive in toothpastes and some mouthwashes, as a tooth decay preventive ingredient.

Why is Fluoride Used?

Fluoride is used to fight tooth decay in children. The key initial studies purporting to demonstrate its effectiveness as an anti-cavity fighting compound were performed back in the 1940s. Those studies, conducted in Grand Rapids, MI in 1945, in Newburgh, NY in 1945, in Brantford, Ontario in 1945, and in Evanston, IL in 1947, are now being called into question. According to Dr. Philip Sutton, author of "The Greatest Fraud: Fluoridation" (*A Factual Book, Lorne, Australia, 1996), these studies are actually of dubious scientific quality.

More recently, other studies attempting to document the effectiveness of fluoride have been conducted. Dr. John Yiamouyiannis examined the raw data from a large study that was conducted by the National Institute for Dental Research (NIDR). He concluded that fluoride did not appear to have any decay preventing success, as there was little difference in the DMFT values (the mean number of decayed, missing or filled teeth) for approximately 40,000 children. It did not matter whether they grew up in fluoridated, non-fluoridated or partially fluoridated communities. (Yiamouyiannis, J.A. "Water Fluoridation and Tooth Decay: Results from the 1986-87 National Survey of U.S. Schoolchildren", *Fluoride*, 23, 55-67, 1990).

A larger study has been conducted in New Zealand. There, the New Zealand National Health Service plan examines the teeth of every child in key age groups, and have found that the teeth of children in non-fluoridated cities were slightly better than those in the fluoridated cities. (Colquhoun, J. "Child Dental Health Differences in New Zealand", *Community Healthy Services*, XI 85-90, 1987).

Although children's teeth have improved steadily from the 1930s to the 1990s, this improvement appears to be independent of the addition of

fluoride to the water. A study has yet to be conducted that specifically addresses whether the addition of fluoride affects the quality of teeth, while controlling and accounting for other factors and other sources of fluoride.

Despite growing questions about the effectiveness of using fluoride to fight tooth decay - and increasing concerns of the safety of this practice - over 60 percent of the United States' water supply is fluoridated. Most of those cities are in the eastern part of the U.S.

What are the Concerns Associated with the Addition of Fluoride to the Water Supply?

The most recognized problem with the ingestion of too much fluoride is dental fluorosis. This condition is characterized by the failure of tooth enamel to crystallize properly in permanent teeth. The effects range from chalky, opaque blotching of teeth to severe, rust-colored stains, surface pitting and tooth brittleness.

This condition, though worrisome, may not be the key concern, at least according to some researchers. Dr. Phyllis Mullenix believes, based on her research, that fluoride acts in a way that lowers the I.Q. of children ("Neurotoxicity of Sodium Fluoride in Rats", Mullenix, P. *Neurotoxicology and Teratology*, 17 (2), 1995).

Dr. William Marcus, believes that a study conducted by Battelle for the National Toxicology Program on the toxicology of fluoride shows that there were dose-related increases in bone cancer in male rats. Dr. Marcus also questions the removal by peer reviewers of cancers at other sites in the rats as well. Especially worrisome to Dr. Marcus is the fact that the levels of fluoride that caused the cancers in the rats were lower than those seen in humans who ingested lower amounts, but for a longer period. These levels are generated because fluoride is accumulated in the body and is not secreted.

Dr. Marcus was formerly the chief toxicologist for the EPA's Office of Drinking Water, but was fired in 1991 after insisting that an unbiased evaluation of fluoride's cancer potential be conducted. Marcus fought his dismissal, and was able to be reinstated after demonstrating in court that it was politically motivated.

An article in the *Irish Times* of Dublin on August 16, 1999, reports that Dr. Hans Moolenburgh's research in Holland found that up to 4 percent of people using fluoridated water experienced health problems. These problems ranged from gastrointestinal disorders to mouth sores to rashes to headaches to forms of arthritis to more serious concerns such as cancers and neurological complaints.

Studies dating back to the 1950s have shown links between Down's Syndrome and natural fluoridation. Ionel Rapaport also showed how the age of women bearing Down's Syndrome children decreased in direct relation to the increase of fluoride in the water supply. The more fluoride that was in the water, the younger the age of the women bearing Down's Syndrome children.

Even those who aren't convinced of the toxicity of fluoride should be concerned about the level of fluoride added to the water supply. The optimum level was set in the 1940s at approximately 1 ppm (equal to 1 mg/l). This was based on assumptions that the total intake of fluoride would be 1 mg/day, assuming 4 glasses of water were drunk per day. However, current intake of fluoride comes not just from the water supply. A study conducted by researchers at the University of Iowa and reported in the November issue of the *Journal of American Dental Association* found that 71% of more than 300 soft drinks contained 0.60 ppm fluoride. Toothpaste, beverages, processed food, fresh fruits and vegetables, vitamins and mineral supplements all contribute to the intake of fluoride. It is now estimated that the total amount of fluoride ingested per day is 8 mg/day, eight times the optimum levels.

An additional and less well studied concern is the interaction of the fluoride compounds added to water with other water additives. Most studies examining the addition of fluoride to water have used sodium fluoride, however, most communities use the less expensive forms such as silicofluoride, hydrofluosilicic acid or sodium silicofluoride. A 1999 study of 280,000 Massachusetts children shows that levels of lead in blood were significantly higher in communities using these cheaper compounds than in towns where sodium fluoride was used or where the water was not treated at all. ("Children's Health and the Environment", *17th International Neurotoxicology Conference*, Little Rock, Arkansas, October 17-20, 1999).

Aluminum compounds are frequently added to the water supply as clarifying agents. On its own, aluminum is not readily absorbed by the body, however, when fluoride is present, the two form aluminum-fluoride, which is easily absorbed. A long term study published in 1988 found that even low levels of aluminum-fluoride in drinking water delivered more aluminum to the brain than concentrated aluminum fluoride. The same study found that low levels of aluminum fluoride and sodium fluoride found in "optimally" fluoridated water cause severe kidney damage and lesions to the brain similar to those found in Alzheimer's and other forms of dementia. Dr. Robert Isaacson, State University of New York, found that when aluminum fluoride is added to the food of rats, the rats developed short-term memory problems, smell sensory loss and other characteristics of Alzheimer's disease. (Isaacson, R. "Rat studies link brain cell damage with aluminum and fluoride in water" *State Univ. of New York, Binghamton, NY, Wall Street Journal* article by Marilyn Chase; Oct. 28, 1992, p. B-6).

What are the Thyroid-Specific Concerns?

Is fluoride in part the reason for near epidemic levels of hypothyroidism in the United States? Some experts and researchers believe this is the case.

Fluoride had been used for decades as an effective anti-thyroid medication to treat hyperthyroidism and was frequently used at levels below the current "optimal" intake of 1 mg/day. This is due to the ability of fluoride to mimic the action of thyrotropin (TSH). It makes sense, then that out of the [over 150 symptoms and associations of hypothyroidism](#), almost all are also symptoms of fluoride poisoning.

Researcher and advocate Andreas Schuld has also found that excess of fluoride correlates with other thyroid-related issues such as iodine deficiency. Fluoride and iodine, both being members of the halogens group of atoms, have an antagonistic relationship. When there is excess of fluoride in the body it can interfere with the function of the thyroid gland. It is possible that iodine deficiency, which is the most common cause of brain damage and mental disability in the world, could be lessened by simply cutting back on the use of fluoride.

The Future of Fluoride

Some advocates believe that the truth about fluoride does not reach the public easily because fluoride, produced as a toxic waste byproduct of many types of heavy industry - such as aluminum, steel, fertilizer, glass, cement and other industries -- must be disposed of somewhere. If it's not used as an additive to water, manufacturers would have to pay millions of dollars to dispose of it properly, so the pressure to keep fluoride listed as a healthy additive to water-and not as an environmental toxin that requires costly disposal - is great and political pressures to keep fluoride in the drinking water is strong.

And the U.S. government has been one of the key supporters for fluoridation. Despite the questions regarding fluoride's effectiveness and safety, the administration's stated federal health objective is to increase the number of Americans with fluoridated tap water from previous levels of 62 percent to 75 percent in 2000.

Given half a century of support for fluoridation, it's also not likely that the American Dental Association will backtrack on its support for fluoridation.

Some cities are taking action, and making the decision to stop fluoridating their water supply - or not to fluoridate in the first place. For example, the City Council of Santa Barbara, California voted in late November of 1999 in favor of a resolution that "disagrees with and rejects the State's recommendation to fluoridate the city's public water system." With this action Santa Barbara joined the California cities of Santa Cruz, El Cajon, La Mesa, Escondido and Helix, Riverview, and Lakeside water districts that have each passed protective resolutions or ordinances in 1999. The cities of San Diego and Sunnyvale have ordinances prohibiting fluoridation that pre-date the State's law. The city officials of Santa Barbara indicated that adding a chemical to the water supply to medicate everyone was not the right approach and requested that the City's staff look into other programs to help children obtain fluoride for dental health.

The only admission that you're likely to see is the 1997 addition of warnings on toothpaste tubes, that now say: "Don't Swallow—Use only a pea-sized amount for children under six." and "Children under six should be supervised while brushing with any toothpaste to prevent swallowing." In areas where the drinking water already contains fluoride, brushing more than once daily with more than a pea-sized amount of fluoridated toothpaste can cause fluorosis, the discoloration and spotting of the teeth that affects an estimated 20% of children.

What Can You Do?

Besides learning more about the effects of fluoride and getting involved in your community's decisions regarding water fluoridation, you can buy an unfluoridated, natural toothpaste, such as Tom's of Maine, particularly for young children.

You can also pay attention to the water you drink, and use filtered or bottled waters. Some water filters can remove fluoride from the water, but carbon-based filters such as the Brita filter do not, so be sure to find the right type of filter for fluoride.

Many bottled waters contain no additional fluoride. You can find out the fluoride and other mineral content of your favorite bottled waters at [Bottled Water Web's Bottlers listing](#) [Evian](#), and [Perrier](#), for example, contain no measurable fluoride, but [Calistoga](#) brand has 0.9 parts per million.

FOR MORE INFORMATION: Thyroid-Specific References

[Bibliography -- Studies Dealing with Thyroid and Fluoride](#)
[PubMed Search at National Library of Medicine on Thyroid/Fluoride Connection](#)

FOR MORE INFORMATION: Fluoride Around About.com

[Fluoride-related links from John Brooke - About.com's Guide to Dentistry](#)
[How Fluoride Works, from John Brooke - About.com's Guide to Dentistry](#)
[Fluoride -- Nutrition Profile -- from Rick Hall, About.com's Nutrition Guide](#)

FOR MORE INFORMATION: Fluoride-Related Information

[Encyclopedia Britannica on Fluoridation](#)
[Gary Null, PhD - Information and a plan for action to stop fluoridation](#)
[Preventive Dental Health Association David Kennedy, DDS - The Dangers of Fluoridation & Alternatives to Fluoride](#)
[Elke Babiuk - Fluoride: Protected Pollutant or Panacea? \(includes photos of fluorosis and lots of abstracts\)](#)
[The Fluoride Stop by Andreas Schuld](#)
[Stop Fluoridation USA by Darlene Sherrill](#)
[Scholarly Journal of the International Society for Fluoride Research](#)
[Fluorides and Fluoridation, Leading Edge Research Group by Val Verlerian](#)
[Fluoride Issues - Dan Montgomery](#)
[America Overdosed on Fluoride - Lynn Landes](#)
[The Dangers of Fluoride and Fluoridation by Michael Schacter, MD](#)
[Fluoridaton Debate \(Environmental Health Perspectives Volume 105, Number 11, November 1997\)](#)
[Fluoridation: The overdosing of America - Fact or Fiction? slides by Gerald H. Smith, DDS](#)
[Fluoridation for Dummies - Oregon Citizens for Safe Water](#)
[An Association of State and Local Websites STOP Fluoridation of North Hollywood, California](#)
[Darryl W. Roundy, D.C. - Fluoride Research](#)
[Fluoride: Commie Plot or Capitalist Ploy by Joel Griffiths, investigative reporter](#)
[Fluoride: Wide Range of Serious Health Problems by Shirley Lipschutz-Robinson](#)
[Mark Spess - The Fluoride Detective](#)
[Fluoride - Friend or Fraud, Liberty Australia](#)
[Fluoride Controversy -- The Townsend Letter for Doctors and Patients](#)
[Citizens for Safe Drinking Water \(Mountainview CA\)](#)
[Fluoridated Toothpastes must now be labeled "POISON" by Charlotte Gerson](#)
[Fluoride: Public Health Goal](#)
[Did Government Approve Citizens as Toxic Waste Sites? \(search site for "fluoride"\)](#)
[Scientific Facts on the Biological Effects of Fluorides](#)
[California Lawsuit \(L.A. Citizens for Safe Drinking Water\)](#)
[Fluoridation / Fluoride Toxic Chemicals In Your Water](#)

A crack appears in the fluoride front -- After surveying the growing evidence, a high-profile advocate has second thoughts about the safety of fluoride.

By Michael Downey Special to the Toronto Star April 25 , 1999

Two years ago, parents in the United States began noticing the word poison on their toothpaste tubes. The reason: U.S. drug regulators were beginning to doubt the safety of fluoride, particularly to children, and demanded warnings on the labels.

Health Canada has not followed the U.S. lead, although fluoride toothpaste here does carry a mild warning to avoid swallowing it. But attitudes toward fluoride in this country are also beginning to change.

Dr. Hardy Limeback is a leading Canadian fluoride authority who is often cited by health officials in their defense of fluoridated water. He is also a long-standing consultant to the Canadian Dental Association and a professor of

dentistry at the University of Toronto.

But in an interview last week, he conceded that fluoride may be destroying our bones, our teeth and our overall health. Although he still believes fluoride in toothpaste is effective against tooth decay, he says it doesn't need to be added to our water and we may be taking unnecessary risks by doing so.

"There is no point swallowing fluoridated water. The only benefit comes with direct contact with the teeth."

"Torontonians have double the fluoride levels in their hip bones compared to Montreal, where water is not fluoridated." What effect these high fluoride deposits in our bones will have is unclear, he says, "but we know that in areas of the world where water is naturally high in fluoride, skeletal fluorosis is a widespread problem." Skeletal fluorosis is a debilitating condition that occurs when fluoride accumulates in bones, making them extremely weak and brittle. In parts of China, India and Turkey where water is naturally high in fluoride, residents tend to age early and die before the age of 50, weak, arthritic and hunched over. "Old" men of 30 drag themselves around, leaning on sticks; their bones shatter like glass when they fall. Women give birth to dead babies after pregnancies of only four months.

Children under three should never use fluoridated toothpaste. Or drink fluoridated water. And baby formula must never be made up using Toronto tap water. Never. The earliest symptom? Mottled and brittle teeth, a condition known as dental fluorosis. The condition weakens teeth, making them porous and thus easily stained. The mottled spots start off white but typically turn brown. It's permanent and recurring, and treating it is very costly.

If this description sounds familiar, there's a good reason. Limeback says "most" of the children he treats in his Mississauga practice suffer dental fluorosis, and by some estimates, 60 per cent of all children living in fluoridated areas have it.

What causes it in these children is not just the water. Young children do not have the reflexes to avoid swallowing toothpaste when brushing their teeth. Some even enjoy the taste of it. And because they're developing rapidly, children are more susceptible to the negative effects of fluoride buildup.

"Children under three should never use fluoridated toothpaste. Never. In fluoridated areas, people should never use fluoride supplements. We tried to get them banned for children but (the dentists) wouldn't even look at the evidence we presented," says Limeback, emphasizing that we are now spending more treating dental fluorosis than we would spend treating cavities if water were not fluoridated.

For decades, anti-fluoride activists have blamed fluoride (which is only slightly less poisonous than arsenic) for a variety of problems, including osteoporosis, bone cancer, kidney problems, arthritis, genetic damage and birth defects, premature aging, lowered intelligence, and Attention Deficit Hyperactive Disorder.

Although there are numerous studies suggesting links between fluoride and various illnesses, pro-fluoridationists have always contended - correctly - that the exact effects of long-term fluoridation on our bodies have not been established beyond a shadow of a doubt.

As Chris Clark, a high-profile fluoride booster and professor of dentistry at the University of British Columbia, says, "There is no proof that fluoride causes brittle bones or cancer," at current concentrations. (Toronto's water supply is 1 part per million (ppm) fluoride. Toothpaste, typically, contains 1,500 ppm.) Limeback, who until very recently would have been considered an ally of Clark's, vehemently disagrees. "We absolutely know about the tragic consequences of higher levels of fluoride, and we know it builds up over time. These people haven't done any studies to find out what effect fluoride accumulation will have at current levels. How can they say it's safe when the studies haven't been done? Right now, we have people who have been ingesting fluoride for 35 years."

Limeback points out that almost all the beverages we drink (beer, pop, juice) are made with fluoridated water. Fish and other foods also contain fluoride. Many of the vegetables we eat are fertilized with compounds containing fluoride; they are irrigated with, and washed and cooked in, fluoridated water. So we are getting far more fluoride than it appears.

And, considering safe fluoride levels in terms of concentrations (parts per million) is a dubious practice, since at least half the fluoride we ingest fuses with bones and teeth and never leaves the body.

So although a big one-time dose of fluoride can kill - as happened to a New York boy during a fluoride treatment and to people in Alaska when too much fluoride was accidentally added to the water - Limeback says it's the cumulative effect we should be most worried about.

Contrary to popular belief, there is no proof that fluoride fights cavities. In the U.S., the government recently ordered toothpaste manufacturers to stop claiming it does until they could prove it. (None bothered to try.)

(This may seem ironic, given that companies who want to market new drugs must prove they are safe first whereas a drug already in our water will stay there until we prove it isn't safe.)

Absolute proof may be hard to come by, but the evidence is abundant and compelling. A U.S. study showed a link to bone and liver cancer.

A half dozen studies in the Journal of the American Medical Association show more hip fractures in fluoridated areas - up to 300 per cent more, according to one report. Appearing on a recent Canadian television show, a former scientist with the Environmental Protection Agency called fluoridation "the biggest fraud of the century."

Dr. Richard Foulkes, special consultant to the B.C. Minister of Health. Both later reversed their recommendations. Wrote Colquhoun in 1982: "Common sense should tell us that if a poison circulating in a child's body can damage tooth-forming cells, then other harm is also likely."

In the final analysis, perhaps the proof is in the water. So, does Limeback drink tap water?

I purchase distilled water at a local drugstore and we use it for all our beverage needs,"he says. "Look, I've been drinking fluoride for 35 years and I'm worried.

I have joint problems which cleared up when I switched to non-fluoridated water . . . fluoride is a pollutant, so why would you want to swallow that stuff?"

Michael Downey is a Toronto freelance writer.

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Green Tea, Fluoride, and the Thyroid

by Andreas Schuld
Parents of Fluoride Poisoned Children
Vancouver, BC, Canada

September 10, 2000

I am writing this letter with the intent to inform on various issues associated with the use of fluorides, especially as it relates to green and black teas, and to voice our concern about the continued promotion of green tea as a drink "beneficial to one's health" on your radio show "Current Health Issues".

Tea is very high in fluoride content. Fluoride in tea is much higher than the Maximum Contaminant Level (MCL) set for fluoride in drinking water.

Tea leaves accumulate more fluoride (from pollution of soil and air) than any other edible plant (1,2,3). Fluoride content in tea has risen dramatically over the last 20 years, as has tea consumption (4).

While in 1976 a Belgian analysis showed content of between 50 and 125 ppm fluoride in 15 varieties of tea (3), a Polish study in 1995 found fluoride content of up to 340 ppm in 16 varieties of black tea (5). A major Canadian study published in 1995 reports average fluoride content in tea to be 4.57 mg/l in the 1980's.(6)

A website by a pro-fluoridation infant medical group lists a cup of black tea to contain 7.8 mgs of fluoride (7), which is roughly the same amount as if one were to drink 7.8 litres of water in an area fluoridated at 1ppm. It is well known that fluoride in tea gets absorbed by the body similarly as the fluoride in drinking water (1,8).

Some British and African studies from the 1990's showed a daily fluoride intake of between 5.8 mgs and 9 mgs a day from tea alone.(9,10,11)

In order to understand a dose/concentration relationship properly, one needs to realize that the level of fluoride at 1 part-per-million (ppm) = 1 mg/l was set in the 40's

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when TOTAL intake was considered to be only about 1 mg/day in areas with fluoridated water. It was thought that the fluoridation of water supplies at 1 ppm (1 mg/l) would duplicate this intake, assuming that people would drink 4 glasses of water a day. However, average current total intake of fluorides is approaching the 8mg/day range, according to the last official data available from the US PHS (1991) and other publications (12).

TOTAL intake from ALL sources is the amount to be considered for any adverse health effect evaluation. (13,14,15)

The fact that fluorides accumulate in the body is the reason why a MCL for fluoride content in water needs to be set by the US Environment Protection Agency (EPA) - by law under the US Surgeon General. This is to be done specifically to avoid a condition known as Crippling Skeletal Fluorosis (CSF).

The MCL is set so as to only avoid the third and crippling stage of this disease. It is set at 4ppm => 4mg/liter, assuming that people will retain half of this amount (2mg), and therefore be at a "safe" level. The EPA scientists, whose job and legal duty it is to set the MCL, declared that this level was set fraudulently by outside forces, and that 90% of the data showing the mutagenic properties of fluoride were omitted. (16)

Virtually every company selling green tea advertises it's high fluoride content as "beneficial" in preventing cavities, promulgating the misleading and false data supplied for the last 50 years by the ADA/CDA and other dental health trade organizations, as well as various public health agencies. There are NO double-blind studies anywhere proving the efficacy of fluoride as a caries preventative (17). There ARE double-blind studies proving adverse health effects, at the level of 1ppm (1mg/l) in water.(18) There are no studies documenting safety at any intake level..

Thyroid Medication

Drinking a cup of tea with fluoride content as mentioned above (7.8mg) would mean a fluoride intake much higher(!) than amounts which were actually given as medication to treat hyperthyroidism (-> over-functioning thyroid) for numerous decades - in several countries - specifically to reduce thyroid activity! [(2 -10 mg NaF/day => 0.9mg - 4.5mg F-)] (19,20,21,22)

In the 1930's May reported having _successfully_ treated 1,158 hyperthyroid patients within 6 years with either sodium fluoride or fluorothyrosine, given per mouth. Among products later released on the market were Pardinon and Tyrosin (23, 24). Checking an older Merck Index will verify this information.(25) Gorlizer von Mundy treated patients for more than 30 years in baths containing HF (30ccHF in 200 l water). Later fluorides were deemed not "reliable enough" to be recommended as an antithyroid (26).

RE: CANCER AND GREEN TEA

While there can be no doubt as to the beneficial effects of individual antioxidants found in green tea, the same cannot be said about green tea as a beverage. Existing studies tend to concentrate on active ingredients of green tea, such as epigallocatechin gallate (EGCG), a compound that belongs to a family of antioxidants known

as polyphenols. EGCG and other polyphenols are constituents of tea - especially of green tea.

However, no studies exist investigating the effects of fluorides on these anti-oxidants. Existing studies involving other antioxidants and fluoride compounds give evidence that fluorides can adversely affect the action of antioxidants(27). Thus, while isolated antioxidants may slow down the development of some forms of cancer in experimental studies, their effect may be annihilated in their complex natural environment (as a sum of the action of all the substances present).

Several reviews of available data seem undecided in their conclusions as to the inhibition of carcinogenesis in experimental animals by tea or tea compounds. Data reviewed by Blot et al. (28) suggest "at most a modest benefit, since there is considerable international variation in tea consumption but generally small differences in cancer rates...More relevant case-control and cohort studies show mixed results."

Other epidemiological and human studies have also shown varying results. In a review by Bushman (29) thirty-one human studies and four reviews were examined. Among five studies reporting on **colon cancer**, three found an inverse association and one reported a positive association.

For **rectal cancer**, only one of four studies reported an inverse association; increased risks were seen in two of the studies. An inverse association was suggested for urinary bladder cancer in two of two studies.

While **lung cancer studies** have shown an inverse effect with Okinawan tea, a tentatively increased risk was shown in another study, clearly indicating that more research into this matter is needed. In a recent study on Finnish men, published in 1998 by Terry Hartman and others, again a positive correlation between colon cancer and tea intake was found. Colon cancer occurrence increased with higher intake (30).

Many available green tea/cancer studies last only a few months, and do not take into account the cumulative effects of fluoride, which is a known cancer promoter, and has the ability to transform healthy cells into cancerous ones. (1,17,35,36) For any conclusive evidence to be obtained this must be considered, for long time fluoride ingestion has been shown to cause cancer, especially osteosarcomas and uterine cancer. (31,32)

Dean Burk, for many decades Chief Chemist at the National Cancer Institute, testified at congressional hearings in 1981 stating that over 40,000 cancer deaths in that year were attributable to fluoridation (33). He has said that no chemical causes as much cancer, and faster, than fluorides (34). Public health officials are quick to say that this data is not verified, which is entirely untrue, for international research as well as congressional hearings and court proceedings HAVE verified this information. (1,2,16,17,31,32,33,34,35,36,37,38)

Dental fluorosis (mottled teeth) is the first visible sign of fluoride poisoning.

Studies conducted on tea consumption in Tibetan children by Cao et al. found both dental (51.2%) and

skeletal (32.83%) fluorosis, mainly as a result from drinking brick tea, also known as milk tea (39). More studies by Cao and others reported similar results (40,41) as did a study from Chile showing dental fluorosis risks in 22.1% of the children consuming tea as a main beverage (42). Many similar studies on tea as well as other beverages have been published in the journals of the American Dental Association (ADA) or American Medical Association (AMA) themselves.

Studies on hydrofluoric-acid workers from an electronics company documented that, among the influences of fluorine-containing foodstuff on fluoride content in the biological fluids, the effect of black tea and/or green tea intake was "particularly remarkable". Measuring the urine and serum levels of fluorine ion, in the case of the non-hydrofluoric-acid workers, the concentration increased to about double of the control value. Similarly in a diet test on volunteers, the concentration increased about six times. (43)

There are several other factors to consider regarding fluoride content in tea. One is the amount of fluoride leeching over time. Chinese teas continue to release F- throughout the first hour of infusion, whereas release of F- from Ceylon/Indian teas is essentially completed after 5 minutes.(44)

The first study to investigate fluoride content in decaffeinated teas found an even higher fluoride content in those teas as compared to their caffeinated counterparts. (45) It is thought that this is due to the high fluoride content in the water involved in the de-cafeination process, which then would also make coffee similarly decaffeinated high in fluoride content.

In addition, **the caffeine in tea has a great augmentative effect on the bio-availability of fluoride.** In 1990 researchers at the University of Texas even theorized that "the rise in incidence of dental fluorosis in North America is mainly due to the replacement of water intake by caffeine-containing beverages among the young population".(46) In 1990 German researchers wrote that "continuous intake of black tea rich in fluorides leads to distinct increase of fluoride content of temporary teeth. This is to consider analogous a caries prophylaxis."(47)

Considering this, and tea market statistics which report that, "on any given day, nearly 127 million people -- half of all Americans -- are drinking tea", and that tea is available in 80% of US households (4), one must seriously ask why anyone in their right mind would want to add to the already existing load by adding fluorides to the public water supply.

Fluoride and Aluminum in Tea

To make matters much worse for human health, fluorides in teas are found together with aluminum. The combination of aluminum and fluorides in tea is of urgent concern, due to the increased damage done by fluorides when in the presence of aluminum, especially neurological and renal damage)(17).

A study by Wei and others reported a high correlation ($r = 0.81$) found between the released F and Al in all tested Chinese, Indian and herbal teas.(48)

Nabrzyski and Gajewska (49) report: "..In the 16

samples of commercially available brands of black teas, the levels of aluminum and fluoride ranged from 445 to 1552 ppm (mean = 897 +/- 264 ppm) and from 30 to 340 ppm (mean 141 +/- 85 ppm), respectively. In six herbal teas, the mean levels of aluminum and fluoride were lower, and amounted to 218.9 +/- 150.7 ppm and 6.0 +/- 6.9 ppm, respectively..."

That the aluminum present is indeed resorbed in the simultaneous presence of fluoride is shown in a study by Drs. Klaus R. Koch and Colleagues at the University of Cape Town. They examined the urinary excretion of aluminum (which is an indicator of its resorption) in healthy male volunteers after drinking equal volumes (1.2 litres) of tea, coffee or tap water on separate days.

In every case the amount of aluminum excreted over the 12-hour period increased on the day when tea was taken. Their results indicate that tea consumption must be considered in any assessment of the total dietary intake of aluminum in human beings.(50)

A most important study from 1998 conducted at the Nanchang University in China showed that in older rats fed green tea water extract or green tea leaves, the cerebrum calcium contents were significantly decreased and aluminum contents increased. Zinc contents in the cerebrum were also gradually decreased with the increase of tea leaves dose and tea concentration(51). The cerebrum is the portion of the brain (frontal lobes) where thought and higher function reside.(52)

The fluoride/aluminum association is of particular importance as it relates to Alzheimer's Disease.

Aluminum by itself is not readily absorbed by the body. However, in the presence of fluoride ions, the fluoride ions combine with the aluminum to form aluminum fluoride, which is absorbed by the body. In the body, the aluminum eventually combines with oxygen to form aluminum oxide or alumina (53). Alumina is the compound of aluminum that is found in the brains of Alzheimer's disease.

In the brain, protein binds to the alumina, and "that is the key to the plaques and tangles which are the hallmarks of this terrible disease" (54). In a study by Dr. Robert Isaacson at the State University of New York, aluminum fluoride was added to the rats diet. This, contrary to normal expectations, passed through the brain barrier and gave the rats short term memory, smell sensory loss, unsteady gait, and loss of structures of the neo-cortex and hippocampus, all symptoms of Alzheimer's.(53,54,55,56) A Varner and Jensen study conducted with Isaacson confirmed this in 1998.(57)

Free fluorine ions and traces of aluminum form a complex, fluoroaluminate, which stimulates cellular G proteins. Such a complex can form in food, drinking water, in the organism after fluoride ingestion or absorption, or after administration of a vaccine. Susa (58,59) reports that "fluoroaluminate crosses the cell membrane and directly binds to the membrane-associated inactive Ga protein subunits. Within the Ga subunit, fluoroaluminate occupies the position next to GDP.

The resulting Ga-GDP-AlF₄⁻ complex assumes an active state conformation, which resembles that of Ga-GTP complex. Under physiological conditions, Ga-GTP

complex is formed upon activation of seven transmembrane receptors that couple to heterotrimeric G proteins...Both fluoroaluminate-activated and receptor-activated Ga subunits are capable of transmitting intracellular signals that lead to cellular responses."

There are hundreds of G protein-coupled receptors. (60) The thyroid stimulating hormone (TSH) receptor is also coupled to the G protein. The TSH receptor is densely expressed in the thyroid gland and mediates the production and secretion of thyroid hormones. (61) To presume that the fluoroaluminate will not interfere here is simply naive.

There have been hundreds of scientific studies using aluminum/fluoride complexes in the last ten years. A review of the literature by Strunecká and Patocka reveals that aluminofluoride complexes influence all cells and tissues of the human body with "powerful pharmacological efficacy." (62,63)

[This MEDLINE search will return approx. 100 fluoroaluminate-related items:]
[http://www.ncbi.nlm.nih.gov/htbin-post/Entrez/query?db=m&form=6&uid=99 17518&dopt=m&dispmax=20](http://www.ncbi.nlm.nih.gov/htbin-post/Entrez/query?db=m&form=6&uid=99%2017518&dopt=m&dispmax=20)

Neurological Effects of Fluoride

Other numerous studies in the late 1990's have been published documenting the effects of fluoride on the neurological system. (65,66,67,68,69)

They are briefly addressed here in an excerpt from a paper published by the National Treasury Employees Union (NTEU) Local 280, formerly National Federation of Federal Employees Local 2050, representing the approximately 1500 scientists, lawyers, engineers and other professional employees at EPA Headquarters in Washington, D.C.:

"Why EPA'S Headquarters Union of Scientists Opposes Fluoridation"
Issued May 1, 1999 (17):

"In 1995, Mullenix and co-workers showed that rats given fluoride in drinking water at levels that give rise to plasma fluoride concentrations in the range seen in humans suffer neurotoxic effects that vary according to when the rats were given the fluoride - as adult animals, as young animals, or through the placenta before birth.

Those exposed before birth were born hyperactive and remained so throughout their lives. Those exposed as young or adult animals displayed depressed activity. Then in 1998, Guan and co-workers gave doses similar to those used by the Mullenix research group to try to understand the mechanism(s) underlying the effects seen by the Mullenix group. Guan's group found that several key chemicals in the brain - those that form the membrane of brain cells - were substantially depleted in rats given fluoride, as compared to those who did not get fluoride.

"Another 1998 publication by Varner, Jensen and others reported on the brain- and kidney damaging effects in rats that were given fluoride in drinking water at the same level deemed "optimal" by pro-fluoridation groups, namely 1 part per million (1ppm). **Even more pronounced damage was seen in animals that got the fluoride in conjunction with aluminum.** These

results are especially disturbing because of the low dose level of fluoride that shows the toxic effect in rats - rats are more resistant to fluoride than humans.

This latter statement is based on Mullenix's finding that it takes substantially more fluoride in the drinking water of rats than of humans to reach the same fluoride level in plasma. It is the level in plasma that determines how much fluoride is 'seen' by particular tissues in the body. So when rats get 1 ppm in drinking water, their brains and kidneys are exposed to much less fluoride than humans getting 1 ppm, yet they are experiencing toxic effects. Thus we are compelled to consider the likelihood that humans are experiencing damage to their brains and kidneys at the 'optimal' level of 1 ppm."

("Optimum intake" = 1mg/day)

Toothpaste also contains a significant quantity of Al, more so, when packed in Al tubes. (70) That children frequently ingest too much toothpaste is well established and the reason why since April 1997 a poison warning is to be placed on all fluoride-containing toothpastes in the US. It is an absolute disgrace that this is not the same in Canada, especially when the US FDA has issued several Import Alerts and customs detention orders, documenting fluoride amounts double that of permissible content originating in Canada! (71)

Thyroid Hormones

Thyroid hormones are extremely important in the regulation of metabolic processes and brain development. Every cell in the body depends upon thyroid hormones for regulation of their metabolism.

Many of the symptoms documented in the vast literature on the subject of chronic or low-grade fluoride poisoning can be directly related to thyroid functions and disorders. One of the most prominent features of preskeletal fluorosis is the extraordinary general fatigue experienced by most sufferers, a marked weakness usually linked to low activity of the thyroid gland. (2)

This has been reported since the classic 1930's Roholm study on cryolite workers exposed to fluorides, a study which still serves as the basis for occupational fluoride exposure regulations. (73) At the time of Roholm's work the specialized field of "endocrinology" was yet to be recognized as a reputable discipline. Thyroid diseases were poorly understood. From 1940 to 1970, the application of radioiodine improved this understanding immeasurably.

Fragu (74) writes: "The main transformations brought about by this tool were the knowledge of radioiodine uptake mechanisms, basis of its therapeutic effect, complete identification of thyroid hormonesynthesis, serum transport of thyroid hormones and thyroid imaging. More recently immunological and molecular paradigms changed the understanding of thyroid diseases."

It is only in the last two decades during which endocrinology has progressed so rapidly, that **now over 150 symptoms and associations can be identified in hypothyroidism. Almost all correlate with known symptoms of fluoride poisoning.** (74) Most of the double-blind test results of fluoride poisoning found in

Moolenburgh's study on water containing 1ppm of fluoride - which led to the ban of fluoridation in Holland - are now recognized symptoms of hypothyroidism. (75)

The effects of fluoride on the thyroid gland have been studied so extensively, that it baffles the mind how experts on thyroid disease from Harvard or the University of Toronto can claim that fluorides do not affect thyroid gland function, especially when it has been used as medication to do just that! (76)

This stance just defies all knowledge properly gained in the last 70 years of related research. One cannot find any mention of fluorides in ANY current "official" thyroid disease related literature. And this at fluoride intake levels and at dental fluorosis rates as high as they are!

Already in 1940 authors Robert H. Wilson and Floyd DeEds from the United States Department of Agriculture (discussing the role of fluorine in pesticide sprays), wrote:

"Should a spray residue tolerance limit for fluorine be set to protect the normal, the hyperthyroid, or the hypothyroid individual? ... should the tolerance limit take into consideration that in certain areas the public is already exposed to a fluorine intake in the drinking water?"(77)

We have posted over 100 studies documenting the adverse effects of fluoride on the thyroid gland from the last 70 years or so in the Virtual Library on Fluoride Research (78)at:

http://www.bruha.com/fluoride/html/thyroid_studies.htm

Thyroid SIDS and Down Syndrome

A toxicologist in the United Kingdom recently found that perinatal deaths in a fluoridated area was 15% higher than in neighboring non-fluoridated areas. The fluoridated area had a higher socio-economic status and would have been expected to have less perinatal deaths.

The fluoridated area also had a 30% higher rate of Down's Syndrome. (79a) Down's Syndrome is a disease associated with thyroid pathology. (79b) Chile banned fluoridation because of research by the world-reknowned researcher and Nobel price winner, Dr Albert Schatz, which showed a link to infant deaths due to fluoridation.(80) Already in the 1950s, Ionel Rapaport published studies showing links between Down's Syndrome and natural fluoridation.(81)

[In this context an article should be noted which appeared in the October1995 issue of the "Monitor", a publication by the American Psychological Association, which reported of the similarity in neurological signs in Down's Syndrome and Alzheimer's disease.

The link between the two dates back to the 1940s when George Jervis, who later became the first director of New York State Institute for Basic Research in Developmental Disabilities, conducted autopsies on people with Down's syndrome and found they had the same neuropathology as people with Alzheimer's disease. People with Down's syndrome tend to age faster than the general population and suffer a wide range of accompanying health problems--many of which mimic or mask the presence of Alzheimer's disease.(82)]

Thyroid and Learning Disorders

Learning disorders such as Attention Deficit Hyperactivity Disorder (ADHD) did not knowingly exist before the fluoridation of public water supplies began.

In the 1950's ADHD spread rapidly among school children and gained much exposure in the medical science and health literature. In 1963 the US PHS listed dozens of symptoms associated with hyperactivity and officially changed the name to "minimal brain dysfunction".

By the the 1970's some leading authorities noted that this disorder appeared to lie at the root of nearly every type of childhood behaviour problem, and had become the most commonly diagnosed illness among childhood counsellors. (83,84)

In 1987 the American Medical Association acknowledged that minimal brain damage had become the leading disability reported by elementary schools, and "one of the most common referral problems to psychiatry outpatients clinics" (85)

Many studies on thyroid hormones have shown that attention deficit and/or hyperactivity disorders in children are linked to changes in the levels of thyroid hormone in the blood, and that irritability and aggressive behaviour are linked to thyroid hormone levels and hypothyroidism. (86,87,88,89,90,91,92,93,94,95,96,97).

Behaviour disorders have been associated with thyroid function for over 100 years.

In 1997 Aronson and Dodman wrote, "the hypothyroid human patient has been reported to show a wider range of behavioral symptoms. Particularly in the early stages of the disease reduced cognitive function and concentration together with impaired short-term memory may be confused with attention deficit-hyperactivity disorder, and in one study 66% of patients diagnosed with ADBD were found to be hypothyroid.

Supplementing their thyroid levels was largely curative. Visual and auditory hallucinations may result from altered perception and have been misdiagnosed as schizophrenia or psychosis. Other behavioral symptoms have included fear - ranging from mild anxiety to frank paranoia, mood swings and aggression."(98)

Many psychoactive drugs including Prozac, Paxil and Luvox (Littleton) are fluorinated medications. Rohypnol, the infamous date-rape drug, is fluorinated Valium, which is about 20-30 times more potent than Valium alone. In essence, these drugs effect enzyme functions in certain areas of the brain to achieve the desired effect.(99)

Thyroid hormone disorders may induce almost any psychiatric symptom or syndrome, including rage.

Peter Whybrow (100), of the University of Pennsylvania, writes:

"An intimate association between disturbances of thyroid hormone homeostasis and behavior has been recognized for a long time already: Hyper- and hypothyroidism can induce disturbances of mood and intellectual function (in severe cases even psychosis can be mimicked).

Reciprocally many psychiatric disturbances, such as major depression and manic depressive disease have associated with them disturbances of peripheral thyroid hormone metabolism."

Whybrow reports on the successful treatment of psychiatric disorder by supplementing T4 and T3, both of which are reduced in plasma of rats after two months of fluoride administration of 0.1 - 1mg/day.(101)

Recent Chinese studies show that the influence of a high fluoride environment on intelligence can occur early in development such as during the stages of embryonic life or infancy when differentiation and growth are more rapid. Ultramicroscopic study of embryonic brain tissue obtained from termination of pregnancy operations in endemic fluorosis areas showed "differentiation of brain nerve cells were poor, and brain development was delayed."(102,103)

Highly alarming studies and reviews in the last few years have documented the **high accumulation of fluorides in the fetus in countries all over the world.** (104,105,106,107)

Fluoride tends to transfer freely and immediately through the placenta, as has been shown in numerous publications.(108,109)

It is important to note that mother's milk passes on negligible amounts of fluoride in very high fluoride-intake areas, as if "nature" meant to protect the infant.(110)

Thyroid Fluorine Iodine Antagonism

Additionally, a most important factor to consider is the role of fluoride in iodine deficiency disorders (IDD). The antagonistic relationship between fluoride and iodine, being at opposite ends in the halogen group, has been observed in many studies ever since Wagner von Jauregg began a mass iodine-supplementation program in Austrian areas endemic with goiter (enlargement of the thyroid gland) in the 1920's. (112) The late George Waldbott (2) wrote that when the total iodine pool in the body is low, fluoride interferes with the function of the thyroid gland and thereby produces a fluoride-iodine antagonism, a view shared and documented by numerous others. (113,114)

However, **it has become clear within the last decade that fluoride excess, combined with iodine excess also exert "severe damage to the human body".** (115, 116) In the study by Yang et al.(116) on children's intelligence in high iodine and fluorine regions, the percentage of low-intelligence children was 16.7% at dental fluorosis rates of 72.9%. This is comparable to fluorosis rates we see in North America, some of which are up to 80%. (117)

A study published this year on endemic goiter occurrences in the absence of iodine deficiency again showed higher goiter rates in high-fluoride areas in South Africa.(118)

Could it be that the world-wide "iodine deficiency" is actually fluoride excess? By comparing IDD data supplied by the WHO (119) with fluorosis data found on MEDLINE an answer may be found. You may judge for yourself:

COUNTRY

IDD/GOITER FLUOROSIS

India

Very High (Endemic)
Very High (Endemic)

Nigeria

High
High

Belgium

Moderately Low
Moderately Low

France

Low (3.9%)
Low (3%)

China

Very High (endemic)
Very High (endemic)

Mexico

Very High (>60% San Luis Potosi)
Very High (>60% San Luis Potosi)

Brazil

High (>30%)
High (>30%)

Italy

High (Mean 39%)
High (45% in fl.areas)

Tanzania

Very High (>60%)
Very High (60%)

Sudan

High
High

While it is well known that goiter and hypothyroidism occur more often in mountainous areas, the same has now been shown for dental fluorosis.(120,121)

[Note:While checking for IDD/Goiter data for the US, we discovered that a national survey has never been conducted. The only Canadian data available dates back 30 years, and mentions earlier goiter occurrences in the Great Lakes area. (Brantford (Great Lakes) was the first Canadian city to be fluoridated.))

Meanwhile, "iodine deficiency" is now recognized as the most common cause of preventable brain damage and mental disability in the world today. It affects the brain development of the fetus. All thyroid disorders, including hypothyroidism, can develop already in the fetus.

Regarding the findings by Dr. Phyllis Mullenix (65), and her observation that those exposed to fluorides before birth were born hyperactive and remained so throughout their lives, it fits very neatly with existing research on

hypothyroidism:

"Hypothyroidism that is present from birth is referred to as congenital hypothyroidism (CH). In North America, CH occurs in about 1 in 4000 live-born babies. The majority (over 90%) of affected babies in North America have a permanent, life-long type of CH".(122)

Another thyroid/fluoride connection can be seen in Jennifer Luke's data (123) which has shown that **fluoride accumulates in the pineal gland and inhibits its production of melatonin**. Luke showed in test animals that this inhibition causes an earlier onset of sexual maturity, an effect already reported in humans as well in 1956, as part of the Kingston/Newburgh study. In fluoridated Newburgh, young girls experienced earlier onset of menstruation than girls in non-fluoridated Kingston (124).

The early onset of sexual puberty is a well established symptom of thyroid hormone dysfunction. Usually patients with low thyroid hormones also have deficient secretion of growth hormone, and may have deficient secretion of the gonadotropins, called LH and FSH, which stimulate puberty and reproduction, and ACTH, which is necessary for cortisol and hydrocortisone secretion by the adrenal gland. (125)

[In the above context it should be noted, that **aluminum fluoride also mimicks the inhibitory action of melatonin**.(126)]

Another symptom of an underactive thyroid condition (or iodine deficiency?) - severe growth disturbances - was observed in 1935 by DeEds and Thomas in children in areas where the water contained F- at 1-2 ppm. (127)

Osteoporosis, Arthritis, and Other Bone Disorders

Left undetected and untreated, thyroid disorder can elevate cholesterol levels, cause long-term organ complications and may lead to irregular menstrual cycles, infertility and worsening osteoporosis.(128,129,130)

Fluorides accumulate in your body. For this reason, as mentioned before, a MCL (Maximum Contaminant Level) must be set for fluoride in the drinking water to avoid Crippling Skeletal Fluorosis (CSF).

The US PHS wrote in 1991 that "fluoride increases the stability of the crystal lattice in bone, but makes bone more brittle... the total quantity of fluoride ingested is the single most important factor in determining the clinical course of skeletal fluorosis; the severity of symptoms correlates directly with the level and duration of exposure."(131)

On page 6 of the same report it states:"Fluoride in the drinking water may increase the risk of elderly men and women breaking bones"..pages 56-57: "The weight of evidence from these experiments suggests that fluoride added to water can increase the risk of hip fracture in both elderly women and men...If this effect is confirmed, it would mean that hip fracture in the elderly would replace dental fluorosis as the most sensitive endpoint of fluoride exposure".

Since then several more studies have been published, all showing **greater incidence of hip fractures among**

the elderly in fluoridated areas. (132,133,134) The elderly are also the population suffering greatest from hypothyroidism.

To understand the implications of fluoride in bone disorders:

If you drink 1 cup (6oz) of green/black tea a day, with F- content of 5mg, you can expect Chronic Skeletal Fluorosis to appear as follows (135):

(100lbs. person)

Phase 1:.....within 5 years

(sporadic pain; stiffness in joints; osteosclerosis of pelvis and vertebral column)

Phase 2:.....after 10 years

(chronic joint pain; arthritic symptoms; slight calcification of ligaments; increased osteoclerosis/cancellous bones; with/without osteoporosis of long bones)

Phase 3 (crippling fluorosis).....after 23 years

(limitation of joint movement; calcification of ligaments/neck, vert. Column; crippling deformities/spine major joints; muscle wasting;neurological defects/compression of spinal chord).

Comparing intake levels as high as they are (12) with statistical data, it must become clear that this is already happening to a significant portion of the population.

CONCLUSION:

As argued by Dean Burk and the attorneys who established the connection between cancer deaths and fluoridation, there is a premise in logic which states that the most obvious cause of an event must be taken as face value while one searches for alternative possibilities.

Because it can be documented that fluorides were given as medication for hyperthyroid patients it should be considered the OBVIOUS cause for hypothyroidism and other thyroid-hormone function-related disorders, including ADHD, arthritis, osteoporosis, etc., especially at intake levels as high as they are.

Fluoride poisoning can be observed in large groups of the population, in the form of hypothyroidism. In 1995 one publication (see 127) on hypothyroidism reported that 41 percent of women had fatigue for no obvious reason in the past year. Of these women, 57 percent said they experience fatigue three or more times a week. More than half of women (51 percent) had experienced three or more symptoms commonly associated with hypothyroidism over the past year.

Other symptoms/associations of hypothyroidism include loss of libido, carpal tunnel syndrome, arthritis, lupus, fibromyalgia, memory loss, etc. [For a more complete list, please see (74)]

Dental fluorosis is the first visible indicator that severe thyroid hormone dysfunction has occurred and is occurring. It is NOT a mere cosmetic effect as the dental profession would like us to believe. The

evidence is staggering.

We must take immediate action to protect our children's mental and physical health from the ever-increasing fluoride intake. Water fluoridation must be halted, all foods must be labelled for F- content, and emissions by industry must be strictly regulated.

Overall fluoride intake must be radically reduced.

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Green Tea, Fluoride, and the Thyroid

I am writing this letter with the intent to inform on various issues associated with the use of fluorides, especially as it relates to green and black teas, and to voice our concern about the continued promotion of green tea as a drink "beneficial to one's health" on your radio show "Current Health Issues". Tea is very high in fluoride content. Fluoride in tea is much higher than the Maximum Contaminant Level (MCL) set for fluoride in drinking water. Tea leaves accumulate more fluoride (from pollution of soil and air) than any other edible plant (1,2,3). Fluoride content in tea has risen dramatically over the last 20 years, as has tea consumption (4). While in 1976 a Belgian analysis showed content of between 50 and 125 ppm fluoride in 15 varieties of tea (3), a Polish study in 1995 found fluoride content of up to 340 ppm in 16 varieties of black tea (5). A major Canadian study published in 1995 reports average fluoride content in tea to be 4.57 mg/l in the 1980's.(6) A website by a pro-fluoridation infant medical group lists a cup of black tea to contain 7.8 mgs of fluoride (7), which is roughly the same amount as if one were to drink 7.8 litres of water in an area fluoridated at 1ppm.

It is well known that fluoride in tea gets absorbed by the body similarly as the fluoride in drinking water (1,8). Some British and African studies from the 1990's showed a daily fluoride intake of between 5.8 mgs and 9 mgs a day from tea alone.(9,10,11) In order to understand a dose/concentration relationship properly, one needs to realize that the level of fluoride at 1 part-per-million (ppm) = 1 mg/l was set in the 40's when TOTAL intake was considered to be only about 1 mg/day in areas with fluoridated water. It was thought that the fluoridation of water supplies at 1 ppm (1 mg/l) would duplicate this intake, assuming that people would drink 4 glasses of water a day. However, average current total intake of fluorides is approaching the 8mg/day range, according to the last official data available from the US PHS (1991) and other publications (12). TOTAL intake from ALL sources is the amount to be considered for any adverse health effect evaluation. (13,14,15) The fact that fluorides accumulate in the body is the reason why a MCL for fluoride content in water needs to be set by the US Environment Protection Agency (EPA) - by law under the US Surgeon General. This is to be done specifically to avoid a condition known as Crippling Skeletal Fluorosis (CSF). The MCL is set so as to only avoid the third and crippling stage of this disease. It is set at 4ppm => 4mg/liter, assuming that people will retain half of this amount (2mg), and therefore be at a "safe" level. The EPA scientists, whose job and legal duty it is to set the MCL, declared that this level was set fraudulently by outside forces, and that 90% of the data showing the mutagenic properties of fluoride were omitted. (16) Virtually every company selling green tea advertises it's high fluoride content as "beneficial" in preventing cavities, promulgating the misleading and false data supplied for the last 50 years by the ADA/CDA and other dental health trade organizations, as well as various public health agencies. There are NO double-blind studies anywhere proving the efficacy of fluoride as a caries preventative (17). There ARE double-blind studies proving adverse health effects, at the level of 1ppm (1mg/l) in water.(18) There are no studies documenting safety at any intake level.. Thyroid Medication Drinking a cup of tea with fluoride content as mentioned above (7.8mg) would mean a fluoride intake much higher(!) than amounts which were actually given as medication to treat hyperthyroidism (-> over-functioning thyroid) for numerous decades - in several countries - specifically to reduce thyroid activity! [(2 -10 mg NaF/day => 0.9mg - 4.5mg F-)] (19,20,21,22) In the 1930's May reported having _successfully_ treated 1,158 hyperthyroid patients within 6 years with either sodium fluoride or fluorothyrosine, given per mouth. Among products later released on the market were Pardinon and Tyrosin (23, 24). Checking an older Merck Index will verify this information.(25) Gorlizer von Mundy treated patients for more than 30 years in baths containing HF (30ccHF in 200 l water). Later fluorides were deemed not "reliable enough" to be recommended as an antithyroid (26). RE: CANCER AND GREEN TEA While there can be no doubt as to the beneficial effects of individual antioxidants found in green tea, the same cannot be said about green tea as a beverage. Existing studies tend to concentrate on active ingredients of green tea, such as epigallocatechin gallate (EGCG), a compound that belongs to a family of antioxidants known as polyphenols. EGCG and other polyphenols are constituents of tea - especially of green tea. However, no studies exist investigating the effects of fluorides on these anti-oxidants. Existing studies involving other antioxidants and fluoride compounds give evidence that fluorides can adversely affect the action of antioxidants(27). Thus, while isolated antioxidants may slow down the development of some forms of cancer in experimental studies, their effect may be annihilated in their complex natural environment (as a sum of the action of all the substances present). Several reviews of available data seem undecided in their conclusions as to the inhibition of carcinogenesis in experimental animals by tea or tea compounds. Data reviewed by Blot et al. (28) suggest "at most a modest benefit, since there is considerable international variation in tea consumption but generally small differences in cancer rates...More relevant case-control and cohort studies show mixed results." Other epidemiological and human studies have also shown varying results. In a review by Bushman (29) thirty-one human studies and four reviews were examined. Among five studies reporting on colon cancer, three found an inverse association and one reported a positive association. For rectal cancer, only one of four studies reported an inverse association; increased risks were seen in two of the studies. An inverse association was suggested for urinary bladder cancer in two of two studies. While lung cancer

studies have shown an inverse effect with Okinawan tea, a tentatively increased risk was shown in another study, clearly indicating that more research into this matter is needed. In a recent study on Finnish men, published in 1998 by Terry Hartman and others, again a positive correlation between colon cancer and tea intake was found. Colon cancer occurrence increased with higher intake (30). Many available green tea/cancer studies last only a few months, and do not take into account the cumulative effects of fluoride, which is a known cancer promoter, and has the ability to transform healthy cells into cancerous ones. (1,17,35,36) For any conclusive evidence to be obtained this must be considered, for long time fluoride ingestion has been shown to cause cancer, especially osteosarcomas and uterine cancer. (31,32) Dean Burk, for many decades Chief Chemist at the National Cancer Institute, testified at congressional hearings in 1981 stating that over 40,000 cancer deaths in that year were attributable to fluoridation (33). He has said that no chemical causes as much cancer, and faster, than fluorides (34). Public health officials are quick to say that this data is not verified, which is entirely untrue, for international research as well as congressional hearings and court proceedings HAVE verified this information. (1,2,16,17,31,32,33,34,35,36,37,38) Dental fluorosis (mottled teeth) is the first visible sign of fluoride poisoning. Studies conducted on tea consumption in Tibetan children by Cao et al. found both dental (51.2%) and skeletal (32.83%) fluorosis, mainly as a result from drinking brick tea, also known as milk tea (39). More studies by Cao and others reported similar results (40,41) as did a study from Chile showing dental fluorosis risks in 22.1% of the children consuming tea as a main beverage (42). Many similar studies on tea as well as other beverages have been published in the journals of the American Dental Association (ADA) or American Medical Association (AMA) themselves. Studies on hydrofluoric-acid workers from an electronics company documented that, among the influences of fluorine-containing foodstuff on fluoride content in the biological fluids, the effect of black tea and/or green tea intake was "particularly remarkable". Measuring the urine and serum levels of fluorine ion, in the case of the non-hydrofluoric-acid workers, the concentration increased to about double of the control value. Similarly in a diet test on volunteers, the concentration increased about six times. (43) There are several other factors to consider regarding fluoride content in tea. One is the amount of fluoride leeching over time. Chinese teas continue to release F- throughout the first hour of infusion, whereas release of F- from Ceylon/Indian teas is essentially completed after 5 minutes.(44) The first study to investigate fluoride content in decaffeinated teas found an even higher fluoride content in those teas as compared to their caffeinated counterparts. (45) It is thought that this is due to the high fluoride content in the water involved in the de-caffeination process, which then would also make coffee similarly decaffeinated high in fluoride content. In addition, the caffeine in tea has a great augmentative effect on the bio-availability of fluoride. In 1990 researchers at the University of Texas even theorized that "the rise in incidence of dental fluorosis in North America is mainly due to the replacement of water intake by caffeine-containing beverages among the young population". (46) In 1990 German researchers wrote that "continuous intake of black tea rich in fluorides leads to distinct increase of fluoride content of temporary teeth. This is to consider analogous a caries prophylaxis."(47) Considering this, and tea market statistics which report that, "on any given day, nearly 127 million people -- half of all Americans -- are drinking tea", and that tea is available in 80% of US households (4), one must seriously ask why anyone in their right mind would want to add to the already existing load by adding fluorides to the public water supply. Fluoride and Aluminum in Tea To make matters much worse for human health, fluorides in teas are found together with aluminum. The combination of aluminum and fluorides in tea is of urgent concern, due to the increased damage done by fluorides when in the presence of aluminum, especially neurological and renal damage(17). A study by Wei and others reported a high correlation ($r = 0.81$) found between the released F and Al in all tested Chinese, Indian and herbal teas.(48) Nabrzyski and Gajewska (49) report: "...In the 16 samples of commercially available brands of black teas, the levels of aluminum and fluoride ranged from 445 to 1552 ppm (mean = 897 ± 264 ppm) and from 30 to 340 ppm (mean 141 ± 85 ppm), respectively. In six herbal teas, the mean levels of aluminum and fluoride were lower, and amounted to 218.9 ± 150.7 ppm and 6.0 ± 6.9 ppm, respectively..."

That the aluminum present is indeed resorbed in the simultaneous presence of fluoride is shown in a study by Drs. Klaus R. Koch and Colleagues at the University of Cape Town. They examined the urinary excretion of aluminum (which is an indicator of its resorption) in healthy male volunteers after drinking equal volumes (1.2 litres) of tea, coffee or tap water on separate days. In every case the amount of aluminum excreted over the 12-hour period increased on the day when tea was taken. Their results indicate that tea consumption must be considered in any assessment of the total dietary intake of aluminum in human beings. (50) A most important study from 1998 conducted at the Nanchang University in China showed that in older rats fed green tea water extract or green tea leaves, the cerebrum calcium contents were significantly decreased and aluminum contents increased. Zinc contents in the cerebrum were also gradually decreased with the increase of tea leaves dose and tea concentration (51). The cerebrum is the portion of the brain (frontal lobes) where thought and higher function reside. (52) The fluoride/aluminum association is of particular importance as it relates to Alzheimer's Disease. Aluminum by itself is not readily absorbed by the body. However, in the presence of fluoride ions, the fluoride ions combine with the aluminum to form aluminum fluoride, which is absorbed by the body. In the body, the aluminum eventually combines with oxygen to form aluminum oxide or alumina (53). Alumina is the compound of aluminum that is found in the brains of Alzheimer's disease. In the brain, protein binds to the alumina, and "that is the key to the plaques and tangles which are the hallmarks of this terrible disease" (54). In a study by Dr. Robert Isaacson at the State University of New York, aluminum fluoride was added to the rats diet. This, contrary to normal expectations, passed through the brain barrier and gave the rats short term memory, smell sensory loss, unsteady gait, and loss of structures of the neo-cortex and hippocampus, all symptoms of Alzheimer's. (53,54,55,56) A Varner and Jensen study conducted with Isaacson confirmed this in 1998. (57) Free fluorine ions and traces of aluminum form a complex, fluoroaluminate, which stimulates cellular G proteins. Such a complex can form in food, drinking water, in the organism after fluoride ingestion or absorption, or after administration of a vaccine. Susa (58,59) reports that "fluoroaluminate crosses the cell membrane and directly binds to the membrane-associated inactive G protein subunits. Within the G subunit, fluoroaluminate occupies the position next to GDP. The resulting Ga-GDP-AlF₄- complex assumes an active state conformation, which resembles that of Ga-GTP complex. Under physiological conditions, Ga-GTP complex is formed upon activation of seven transmembrane receptors that couple to heterotrimeric G proteins...Both fluoroaluminate-activated and receptor-activated G subunits are capable of transmitting intracellular signals that lead to cellular responses." There are hundreds of G protein-coupled receptors. (60) The thyroid stimulating hormone (TSH) receptor is also coupled to the G protein. The TSH receptor is densely expressed in the thyroid gland and mediates the production and secretion of thyroid hormones. (61) To presume that the fluoroaluminate will not interfere here is simply naive. There have been hundreds of scientific studies using aluminum/fluoride complexes in the last ten years. A review of the literature by Strunecká and Patocka reveals that aluminofluoride complexes influence all cells and tissues of the human body with "powerful pharmacological efficacy." (62,63) [This MEDLINE search will return approx. 100 fluoroaluminate-related items:] <http://www.ncbi.nlm.nih.gov/htbin-post/Entrez/query?db=m&form=6&uid=9917518&dopt=m&dispmax=20> Neurological Effects of Fluoride Other numerous studies in the late 1990's have been published documenting the effects of fluoride on the neurological system. (65,66,67,68,69) They are briefly addressed here in an excerpt from a paper published by the National Treasury Employees Union (NTEU) Local 280, formerly National Federation of Federal Employees Local 2050, representing the approximately 1500 scientists, lawyers, engineers and other professional employees at EPA Headquarters in Washington, D.C.: "Why EPA'S Headquarters Union of Scientists Opposes Fluoridation" Issued May 1, 1999 (17): "In 1995, Mullenix and co-workers showed that rats given fluoride in drinking water at levels that give rise to plasma fluoride concentrations in the range seen in humans suffer neurotoxic effects that vary according to when the rats were given the fluoride - as adult animals, as young animals, or through the placenta before birth. Those exposed before birth were born hyperactive and remained so throughout their lives. Those exposed as

young or adult animals displayed depressed activity. Then in 1998, Guan and co-workers gave doses similar to those used by the Mullenix research group to try to understand the mechanism(s) underlying the effects seen by the Mullenix group. Guan's group found that several key chemicals in the brain - those that form the membrane of brain cells - were substantially depleted in rats given fluoride, as compared to those who did not get fluoride. "Another 1998 publication by Varner, Jensen and others reported on the brain- and kidney damaging effects in rats that were given fluoride in drinking water at the same level deemed "optimal" by pro-fluoridation groups, namely 1 part per million (1ppm). Even more pronounced damage was seen in animals that got the fluoride in conjunction with aluminum. These results are especially disturbing because of the low dose level of fluoride that shows the toxic effect in rats - rats are more resistant to fluoride than humans. This latter statement is based on Mullenix's finding that it takes substantially more fluoride in the drinking water of rats than of humans to reach the same fluoride level in plasma. It is the level in plasma that determines how much fluoride is 'seen' by particular tissues in the body. So when rats get 1 ppm in drinking water, their brains and kidneys are exposed to much less fluoride than humans getting 1 ppm, yet they are experiencing toxic effects. Thus we are compelled to consider the likelihood that humans are experiencing damage to their brains and kidneys at the 'optimal' level of 1 ppm." ("Optimum intake" = 1mg/day) Toothpaste also contains a significant quantity of Al, more so, when packed in Al tubes. (70) That children frequently ingest too much toothpaste is well established and the reason why since April 1997 a poison warning is to be placed on all fluoride-containing toothpastes in the US. It is an absolute disgrace that this is not the same in Canada, especially when the US FDA has issued several Import Alerts and customs detention orders, documenting fluoride amounts double that of permissible content originating in Canada! (71) Thyroid Hormones Thyroid hormones are extremely important in the regulation of metabolic processes and brain development. Every cell in the body depends upon thyroid hormones for regulation of their metabolism. Many of the symptoms documented in the vast literature on the subject of chronic or low-grade fluoride poisoning can be directly related to thyroid functions and disorders. One of the most prominent features of preskeletal fluorosis is the extraordinary general fatigue experienced by most sufferers, a marked weakness usually linked to low activity of the thyroid gland. (2) This has been reported since the classic 1930's Roholm study on cryolite workers exposed to fluorides, a study which still serves as the basis for occupational fluoride exposure regulations. (73) At the time of Roholm's work the specialized field of "endocrinology" was yet to be recognized as a reputable discipline. Thyroid diseases were poorly understood. From 1940 to 1970, the application of radioiodine improved this understanding immeasurably. Fragu (74) writes:"The main transformations brought about by this tool were the knowledge of radioiodine uptake mechanisms, basis of its therapeutic effect, complete identification of thyroid hormonesynthesis, serum transport of thyroid hormones and thyroid imaging. More recently immunological and molecular paradigms changed the understanding of thyroid diseases." It is only in the last two decades during which endocrinology has progressed so rapidly, that now over 150 symptoms and associations can be identified in hypothyroidism. Almost all correlate with known symptoms of fluoride poisoning.(74) Most of the double-blind test results of fluoride poisoning found in Moolenburgh's study on water containing 1ppm of fluoride - which led to the ban of fluoridation in Holland - are now recognized symptoms of hypothyroidism. (75) The effects of fluoride on the thyroid gland have been studied so extensively, that it baffles the mind how experts on thyroid disease from Harvard or the University of Toronto can claim that fluorides do not affect thyroid gland function, especially when it has been used as medication to do just that! (76) This stance just defies all knowledge properly gained in the last 70 years of related research. One cannot find any mention of fluorides in ANY current "official" thyroid disease related literature. And this at fluoride intake levels and at dental fluorosis rates as high as they are! Already in 1940 authors Robert H. Wilson and Floyd DeEds from the United States Department of Agriculture (discussing the role of fluorine in pesticide sprays), wrote: "Should a spray residue tolerance limit for fluorine be set to protect the normal, the hyperthyroid, or the hypothyroid individual? ... should the tolerance limit take into consideration that in certain areas the public is

already exposed to a fluorine intake in the drinking water?"(77) We have posted over 100 studies documenting the adverse effects of fluoride on the thyroid gland from the last 70 years or so in the Virtual Library on Fluoride Research (78)at:

http://www.bruha.com/fluoride/html/thyroid_studies.htm Thyroid SIDS and Down Syndrome A toxicologist in the United Kingdom recently found that perinatal deaths in a fluoridated area was 15% higher than in neighboring non-fluoridated areas. The fluoridated area had a higher socio-economic status and would have been expected to have less perinatal deaths. The fluoridated area also had a 30% higher rate of Down's Syndrome. (79a) Down's Syndrome is a disease associated with thyroid pathology. (79b) Chile banned fluoridation because of research by the world-rekknowned researcher and Nobel price winner, Dr Albert Schatz, which showed a link to infant deaths due to fluoridation.(80) Already in the 1950s, Ionel Rapaport published studies showing links between Down's Syndrome and natural fluoridation.(81) [In this context an article should be noted which appeared in the October 1995 issue of the "Monitor", a publication by the American Psychological Association, which reported of the similarity in neurological signs in Down's Syndrome and Alzheimer's disease. The link between the two dates back to the 1940s when George Jervis, who later became the first director of New York State Institute for Basic Research in Developmental Disabilities, conducted autopsies on people with Down's syndrome and found they had the same neuropathology as people with Alzheimer's disease. People with Down's syndrome tend to age faster than the general population and suffer a wide range of accompanying health problems--many of which mimic or mask the presence of Alzheimer's disease.(82)] Thyroid and Learning Disorders Learning disorders such as Attention Deficit Hyperactivity Disorder (ADHD) did not knowingly exist before the fluoridation of public water supplies began. In the 1950's ADHD spread rapidly among school children and gained much exposure in the medical science and health literature. In 1963 the US PHS listed dozens of symptoms associated with hyperactivity and officially changed the name to "minimal brain dysfunction". By the the 1970's some leading authorities noted that this disorder appeared to lie at the root of nearly every type of childhood behaviour problem, and had become the most commonly diagnosed illness among childhood counsellors. (83,84) In 1987 the American Medical Association acknowledged that minimal brain damage had become the leading disability reported by elementary schools, and "one of the most common referral problems to psychiatry outpatients clinics" (85) Many studies on thyroid hormones have shown that attention deficit and/or hyperactivity disorders in children are linked to changes in the levels of thyroid hormone in the blood, and that irritability and aggressive behaviour are linked to thyroid hormone levels and hypothyroidism. (86,87,88,89,90,91,92,93,94,95,96,97). Behaviour disorders have been associated with thyroid function for over 100 years. In 1997 Aronson and Dodman wrote, "the hypothyroid human patient has been reported to show a wider range of behavioral symptoms. Particularly in the early stages of the disease reduced cognitive function and concentration together with impaired short-term memory may be confused with attention deficit-hyperactivity disorder, and in one study 66% of patients diagnosed with ADBD were found to be hypothyroid. Supplementing their thyroid levels was largely curative. Visual and auditory hallucinations may result from altered perception and have been misdiagnosed as schizophrenia or psychosis. Other behavioral symptoms have included fear - ranging from mild anxiety to frank paranoia, mood swings and aggression."(98) Many psychoactive drugs including Prozac, Paxil and Luvox (Littleton) are fluorinated medications. Rohypnol, the infamous date-rape drug, is fluorinated Valium, which is about 20-30 times more potent than Valium alone. In essence, these drugs effect enzyme functions in certain areas of the brain to achieve the desired effect.(99) Thyroid hormone disorders may induce almost any psychiatric symptom or syndrome, including rage. Peter Whybrow (100), of the University of Pennsylvania, writes: "An intimate association between disturbances of thyroid hormone homeostasis and behavior has been recognized for a long time already: Hyper- and hypothyroidism can induce disturbances of mood and intellectual function (in severe cases even psychosis can be mimicked). Reciprocally many psychiatric disturbances, such as major depression and manic depressive disease have associated with them disturbances of peripheral thyroid hormone metabolism." Whybrow reports on the

successful treatment of psychiatric disorder by supplementing T4 and T3, both of which are reduced in plasma of rats after two months of fluoride administration of 0.1 - 1 mg/day.(101) Recent Chinese studies show that the influence of a high fluoride environment on intelligence can occur early in development such as during the stages of embryonic life or infancy when differentiation and growth are more rapid. Ultramicroscopic study of embryonic brain tissue obtained from termination of pregnancy operations in endemic fluorosis areas showed "differentiation of brain nerve cells were poor, and brain development was delayed."(102,103) Highly alarming studies and reviews in the last few years have documented the high accumulation of fluorides in the fetus in countries all over the world. (104,105,106,107) Fluoride tends to transfer freely and immediately through the placenta, as has been shown in numerous publications.(108,109) It is important to note that mother's milk passes on negligible amounts of fluoride in very high fluoride-intake areas, as if "nature" meant to protect the infant.(110) Thyroid Fluorine Iodine Antagonism Additionally, a most important factor to consider is the role of fluoride in iodine deficiency disorders (IDD). The antagonistic relationship between fluoride and iodine, being at opposite ends in the halogen group, has been observed in many studies ever since Wagner von Jauregg began a mass iodine-supplementation program in Austrian areas endemic with goiter (enlargement of the thyroid gland) in the 1920's. (112) The late George Waldbott (2) wrote that when the total iodine pool in the body is low, fluoride interferes with the function of the thyroid gland and thereby produces a fluoride-iodine antagonism, a view shared and documented by numerous others. (113,114) However, it has become clear within the last decade that fluoride excess, combined with iodine excess also exert "severe damage to the human body". (115, 116) In the study by Yang et al.(116) on children's intelligence in high iodine and fluorine regions, the percentage of low-intelligence children was 16.7% at dental fluorosis rates of 72.9%. This is comparable to fluorosis rates we see in North America, some of which are up to 80%. (117) A study published this year on endemic goiter occurrences in the absence of iodine deficiency again showed higher goiter rates in high-fluoride areas in South Africa.(118) Could it be that the world-wide "iodine deficiency" is actually fluoride excess? By comparing IDD data supplied by the WHO (119) with fluorosis data found on MEDLINE an answer may be found. You may judge for yourself: COUNTRY IDD/GOITER FLUOROSIS India Very High (Endemic) Very High (Endemic) Nigeria High High Belgium Moderately Low Moderately Low France Low (3.9%) Low (3%) China Very High (endemic) Very High (endemic) Mexico Very High (>60% San Luis Potosi) Very High (>60% San Luis Potosi) Brazil High (>30%) High (>30%) Italy High (Mean 39%) High (45% in fl.areas) Tanzania Very High (>60%) Very High (60%) Sudan High High While it is well known that goiter and hypothyroidism occur more often in mountainous areas, the same has now been shown for dental fluorosis.(120,121) [Note:While checking for IDD/Goiter data for the US, we discovered that a national survey has never been conducted. The only Canadian data available dates back 30 years, and mentions earlier goiter occurrences in the Great Lakes area. (Brantford (Great Lakes) was the first Canadian city to be fluoridated.)] Meanwhile, "iodine deficiency" is now recognized as the most common cause of preventable brain damage and mental disability in the world today. It affects the brain development of the fetus. All thyroid disorders, including hypothyroidism, can develop already in the fetus. Regarding the findings by Dr. Phyllis Mullenix (65), and her observation that those exposed to fluorides before birth were born hyperactive and remained so throughout their lives, it fits very neatly with existing research on hypothyroidism: "Hypothyroidism that is present from birth is referred to as congenital hypothyroidism (CH). In North America, CH occurs in about 1 in 4000 live-born babies. The majority (over 90%) of affected babies in North America have a permanent, life-long type of CH".(122) Another thyroid/fluoride connection can be seen in Jennifer Luke's data (123) which has shown that fluoride accumulates in the pineal gland and inhibits its production of melatonin. Luke showed in test animals that this inhibition causes an earlier onset of sexual maturity, an effect already reported in humans as well in 1956, as part of the Kingston/Newburgh study. In fluoridated Newburgh, young girls experienced earlier onset of menstruation than girls in non-fluoridated Kingston (124). The early onset of sexual puberty is a well established symptom of thyroid hormone dysfunction. Usually patients with low thyroid hormones also have deficient

secretion of growth hormone, and may have deficient secretion of the gonadotropins, called LH and FSH, which stimulate puberty and reproduction, and ACTH, which is necessary for cortisol and hydrocortisone secretion by the adrenal gland. (125) [In the above context it should be noted, that aluminum fluoride also mimicks the inhibitory action of melatonin.(126)] Another symptom of an underactive thyroid condition (or iodine deficiency?) - severe growth disturbances - was observed in 1935 by DeEds and Thomas in children in areas where the water contained F- at 1-2 ppm. (127) Osteoporosis, Arthritis, and Other Bone Disorders Left undetected and untreated, thyroid disorder can elevate cholesterol levels, cause long-term organ complications and may lead to irregular menstrual cycles, infertility and worsening osteoporosis.(128,129,130) Fluorides accumulate in your body. For this reason, as mentioned before, a MCL (Maximum Contaminant Level) must be set for fluoride in the drinking water to avoid Crippling Skeletal Fluorosis (CSF). The US PHS wrote in 1991 that "fluoride increases the stability of the crystal lattice in bone, but makes bone more brittle... the total quantity of fluoride ingested is the single most important factor in determining the clinical course of skeletal fluorosis; the severity of symptoms correlates directly with the level and duration of exposure."(131) On page 6 of the same report it states:"Fluoride in the drinking water may increase the risk of elderly men and women breaking bones".pages 56-57: "The weight of evidence from these experiments suggests that fluoride added to water can increase the risk of hip fracture in both elderly women and men...If this effect is confirmed, it would mean that hip fracture in the elderly would replace dental fluorosis as the most sensitive endpoint of fluoride exposure". Since then several more studies have been published, all showing greater incidence of hip fractures among the elderly in fluoridated areas. (132,133,134) The elderly are also the population suffering greatest from hypothyroidism. To understand the implications of fluoride in bone disorders: If you drink 1 cup (6oz) of green/black tea a day, with F- content of 5mg, you can expect Chronic Skeletal Fluorosis to appear as follows (135): (100lbs. person) Phase 1:.....within 5 years (sporadic pain; stiffness in joints; osteosclerosis of pelvis and vertebral column) Phase 2:.....after 10 years (chronic joint pain; arthritic symptoms; slight calcification of ligaments; increased osteoclerosis/cancellous bones; with/without osteoporosis of long bones) Phase 3 (crippling fluorosis).....after 23 years (limitation of joint movement; calcification of ligaments/neck, vert. Column; crippling deformities/spine major joints; muscle wasting;neurological defects/compression of spinal chord). Comparing intake levels as high as they are (12) with statistical data, it must become clear that this is already happening to a significant portion of the population. CONCLUSION: As argued by Dean Burk and the attorneys who established the connection between cancer deaths and fluoridation, there is a premise in logic which states that the most obvious cause of an event must be taken as face value while one searches for alternative possibilities. Because it can be documented that fluorides were given as medication for hyperthyroid patients it should be considered the OBVIOUS cause for hypothyroidism and other thyroid-hormone function-related disorders, including ADHD, arthritis, osteoporosis, etc., especially at intake levels as high as they are. Fluoride poisoning can be observed in large groups of the population, in the form of hypothyroidism. In 1995 one publication (see 127) on hypothyroidism reported that 41 percent of women had fatigue for no obvious reason in the past year. Of these women, 57 percent said they experience fatigue three or more times a week. More than half of women (51 percent) had experienced three or more symptoms commonly associated with hypothyroidism over the past year. Other symptoms/associations of hypothyroidism include loss of libido, carpal tunnel syndrome, arthritis, lupus, fibromyalgia, memory loss, etc. [For a more complete list, please see (74)] Dental fluorosis is the first visible indicator that severe thyroid hormone dysfunction has occurred and is occurring. It is NOT a mere cosmetic effect as the dental profession would like us to believe. The evidence is staggering. We must take immediate action to protect our children's mental and physical health from the ever-increasing fluoride intake. Water fluoridation must be halted, all foods must be labelled for F- content, and emissions by industry must be strictly regulated. Overall fluoride intake must be radically reduced. Andreas Schuld Parents of Fluoride Poisoned Children (PFPC) Vancouver, B.C., Canada



References:

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GALLIUM

Gallium is a remarkably strange, powerful, and very understudied nutrient. There are ample studies listed below showing that a gallium deficiency might be involved in Graves' disease, ophthalmopathy, autoimmune diseases like lupus, osteoporosis, and cancer. When you look at the whole picture of gallium, it looks like a deficiency of gallium is a key part of Graves' and hyperthyroidism. However, at this point, based upon my personal experimentations with gallium, I'm not sure and can't recommend its use.

This study shows that in Graves' hyperthyroidism, gallium uptake by the thyroid, thymus, and tear glands is accelerated. Is this due to a deficiency of gallium and the thyroid and other organs are preferentially accumulating it to correct the deficiency? I'm not sure.

Title

Thyroid uptake of *gallium* in Graves' disease.

Author

Allard JC; Lee VW; Franklin P

Address

Department of Radiology, Boston University School of Medicine, Boston City Hospital, Massachusetts.

Source

Clin Nucl Med, 13(9):663-6 1988 Sep

Abstract

A patient with hyperthyroid Graves' disease presented with ptosis, leading to a workup for myasthenia gravis. An enlarged thymus gland was noted on computed tomography. **A scan with gallium-67 citrate showed prominent and diffuse thyroid gland activity as well as prominent lacrimal activity.** This finding of thyroid uptake of *gallium* led to the correct diagnosis of Graves' disease. Such a finding has not been reported previously. The associated thymic, thyroid, and orbital findings in Graves' disease are discussed.

The following study states, "Thyroidal gallium-67 uptake has been reported to occur frequently with subacute thyroiditis, anaplastic thyroid carcinoma, and thyroid lymphoma, and occasionally with Hashimoto's thyroiditis and follicular thyroid carcinoma."

Title

Gallium-67 uptake by the thyroid associated with progressive systemic sclerosis.

Author

Sjoberg RJ; Blue PW; Kidd GS

Address

Department of Medicine, Fitzsimons Army Medical Center, Aurora, Colorado 80045-5001.

Source

Am J Med Sci, 297(1):42-5 1989 Jan

Abstract

Although thyroidal uptake of *gallium*-67 has been described in several thyroid disorders, *gallium*-67 scanning is not commonly used in the evaluation of thyroid disease. **Thyroidal gallium-67 uptake has been reported to occur frequently with subacute thyroiditis, anaplastic thyroid carcinoma, and thyroid lymphoma, and occasionally with Hashimoto's thyroiditis and follicular thyroid carcinoma.** A patient is described with progressive systemic sclerosis who, while being scanned for possible active pulmonary involvement, was found incidentally to have abnormal *gallium*-67 uptake only in the thyroid gland. Fine needle aspiration cytology of the thyroid revealed Hashimoto's thyroiditis. Although Hashimoto's thyroiditis occurs with increased frequency in patients with progressive systemic sclerosis, thyroidal uptake of *gallium*-67 associated with progressive systemic sclerosis has not, to our knowledge, been previously described. Since aggressive thyroid malignancies frequently are imaged by *gallium*-67 scintigraphy, fine needle aspiration cytology of the thyroid often is essential in the evaluation of thyroidal *gallium*-67 uptake.

The following study shows gallium accumulation in adenomatous goiter. This could be interpreted that gallium is involved in the etiology of the goiter or that the body has sent the gallium to the site as part of a corrective measure.

Title

Ga-67 citrate accumulation in adenomatous goiter.

Author

Miyamoto S; Kasagi K; Takeuchi R; Hidaka A; Hatabu H; Misaki T; Iida Y; Okanishi S; Konishi J

Address

Department of Nuclear Medicine, Kyoto University, Japan.

Source

Clin Nucl Med, 17(10):803-5 1992 Oct

Abstract

An elderly woman with a diffusely enlarged goiter and multiple miliary nodular lesions on chest x-ray showed Ga-67 accumulation in the right thyroid lobe. Histologic findings obtained after total thyroidectomy and open lung biopsy revealed papillary carcinoma in the left lobe with pulmonary metastases and adenomatous nodules in the right lobe. This is the first report of Ga-67 accumulation in adenomatous goiter.

The following study describes trace mineral function in bone turnover in relation to osteoporosis. Gallium and copper both suppress bone turnover and therefore benefit persons with osteoporosis.

Title

[Effects of essential trace elements on bone turnover--in relation to the osteoporosis]

Author

Okano T

Address

Department of Hygienic Sciences, Kobe Pharmaceutical University.

Source

Nippon Rinsho, 54(1):148-54 1996 Jan

Abstract

Trace Elements are essential for normal growth and development of skeletons in humans and animals. Although they are minor building components in teeth and bone, they play important functional roles in bone metabolism and bone turnover. Fluoride accumulates in new bone formation sites and results in a net gain in bone mass. Aluminum induces impairment of bone formation by the inhibition of osteoblastic function. Magnesium enhances bone turnover by through the stimulation of osteoclastic function. Zinc regulates secretion of calcitonin from thyroid gland and influences on bone turnover. **Gallium suppresses bone turnover in humoral hypercalcemia of malignancy in a similar mechanism as aluminum and cadmium. Copper induces low bone turnover by both suppressions of osteoblastic and osteoclastic functions.** Iodine as the hormonal forms of thyroxine and triiodothyronine enhances bone turnover. Among the trace elements in bone and hair, significant differences were found in the contents of zinc, copper and manganese between normal subjects and osteoporotic patients. However, exact involvements of the trace elements in osteoporosis have not yet been clarified.

The following study sheds more light on gallium's role in building bone. Following gallium administration, increased levels of bone calcium were found. Also gallium accumulates in the active areas of bone formation indicating that it plays an active role in the formation of bone. Another study which indicates a gallium deficiency may be involved in osteoporosis, which we know is a disease which accompanies Graves'.

Title

***Gallium* increases bone calcium and crystallite perfection of hydroxyapatite.**

Author

Bockman RS; Boskey AL; Blumenthal NC; Alcock NW; Warrell RP Jr

Source

Calcif Tissue Int, 39(6):376-81 1986 Dec

Abstract

Gallium, a group IIIa metal, is known to interact with hydroxyapatite as well as the cellular components of bone. In recent studies we have found ***gallium*** to be a potent inhibitor of bone resorption that is clinically effective in controlling cancer-related hypercalcemia as well as the accelerated bone resorption associated with bone metastases. To begin to elucidate ***gallium***'s mechanism of action we have examined its effects on bone mineral properties. After short-term (14 days) administration to rats, gallium nitrate produced measurable changes in bone mineral properties. Using atomic absorption spectroscopy, **low levels of gallium were noted to preferentially accumulate in regions of active bone formation, 0.54 +/- .07 microgram/mg bone in the metaphyses versus 0.21 +/- .03 microgram/mg bone in the diaphyses, P less than 0.001. The bones of treated animals had increased calcium content measured spectrophotometrically.** Rats injected with radiolabeled calcium during ***gallium*** treatment had greater 45-calcium content compared to control animals. By wide-angle X-ray analyses, larger and/or more perfect hydroxyapatite was observed. The combined effects of ***gallium*** on bone cell function and bone mineral may explain its clinical efficacy in blocking accelerated bone resorption.

The following study shows that gallium and zinc are antagonistic minerals which can compete for absorption.

Title

Inhibition of liver, kidney, and erythrocyte delta-aminolevulinic acid dehydratase (porphobilinogen synthase) by ***gallium*** in the rat.

Author

Goering PL; Rehm S

Address

Division of Life Science, Food and Drug Administration, Rockville, Maryland 20857.

Source

Environ Res, 53(2):135-51 1990 Dec

Abstract

Selective inhibition of enzymes in the heme biosynthesis pathway with concomitant urinary excretion of heme precursors serve as potentially important biological markers of chemical exposure and cell injury. Intratracheal administration of ***gallium*** arsenide particulate suspensions has been shown to result in inhibition of delta-aminolevulinic acid dehydratase (ALAD) in several tissues and increased excretion of the heme precursor aminolevulinic acid (ALA). This study was undertaken to evaluate in vivo the role of ***gallium*** alone in ALAD inhibition and increased urinary excretion of ALA. Male CD rats received a single ip injection of Ga₂(SO₄)₃ at doses of 12.5, 25, 50, 100, and 200 mg Ga/kg. A dose-dependent inhibition of ALAD was observed 24 hr later in liver, kidney, and erythrocytes. After injection of 25 mg Ga/kg, maximal inhibition (42 to 49% of control) of ALAD occurred between 6 and 24 hr in liver and kidney with full recovery of activity at 96 hr. In erythrocytes, maximal inhibition (48% of control) occurred between 24 and 48 hr with recovery of activity at 96 hr. Mild to moderate renal proximal tubular necrosis in the pars recta was observed 24 hr after administration of 100 and 200 mg/kg, but no histopathologic changes were evident at lower doses. No consistent changes in urinary excretion of ALA were observed. Lineweaver-Burk analyses of renal and hepatic ALAD activities in the absence and presence of ***gallium*** indicated that the inhibition of ALAD by this element is noncompetitive (same K_m, decreased V_{max}). ***Gallium*** was shown to possess an inhibition constant (K_i) of approximately 3 microns for ALAD, similar to the K_i obtained for lead in other studies. Incubation of ALAD in vitro with ***gallium*** and lead, an active thiol group inhibitor, resulted in a greater inhibition of the enzyme. **Further in vitro studies demonstrated the attenuation of gallium inhibition of hepatic and renal ALAD by zinc, suggesting that the mechanism of gallium action may involve competition for or displacement of zinc from the sulfhydryl group of the enzyme active site.** Since ALAD inhibition occurred at doses at which no histopathologic changes were evident, the determination of ALAD activity in various tissues, including blood, may be of potential value as a biomarker of exposure/toxicity to metals such as ***gallium***. The effect of chemical form and route of exposure of ***gallium*** and effects of other Group III metals on inhibition of ALAD and excretion of ALA is

The following study shows that gallium causes the death of tumor cells because it binds to transferrin, thereby preventing iron from being transported to the tumor cells. It is known that lowering iron levels will suppress tumor growth. Bear in mind that the gallium levels used in this type of experiment far exceed what would be a normal physiological dose. One important lesson from this study is that high levels of gallium can suppress iron levels and we know that iron is essential for proper thyroid function. A small amount of gallium may help but a large amount may impede thyroidal health.

Title

Treatment with *gallium* nitrate: evidence for interference with iron metabolism in vivo.

Author

Seligman PA; Moran PL; Schleicher RB; Crawford ED

Address

Department of Medicine, University of Colorado Health Sciences Center, Denver 80262.

Source

Am J Hematol, 41(4):232-40 1992 Dec

Abstract

Gallium, when bound to transferrin, has been previously shown to cause tumor cell cytotoxicity by preventing cellular uptake of transferrin bound iron in vitro. Patients treated with constant infusion *gallium* nitrate for carcinoma show a rise in serum iron within 6 hr of the start of treatment. Serum iron returns to baseline by 24 hr post-infusion. Atomic analysis of iron and *gallium* content of Sephadex G-150 fractions of treatment sera indicate that about an equimolar amount of *gallium* and iron are associated with transferrin. These *gallium* and iron concentrations result in inhibition of transferrin mediated iron uptake in vitro, and in vivo allow for > 90% saturation of transferrin with metal. All seven patients who completed two courses of *gallium* therapy exhibited hypochromic microcytic anemia (mean fall in hemoglobin 3.5 grams %). Evidence for red cell iron depletion was confirmed by an increase (mean 3.3-fold) in zinc protoporphyrin levels. Since transferrin receptor increases on *gallium* treated iron requiring cells in vitro, we assessed cell surface transferrin receptor on peripheral blood lymphocytes by measuring fluorescent transferrin receptor antibody binding. A population of highly transferrin receptor positive cells peaks at 48 hr into the infusion. DNA analysis as well as double staining indicate the majority of transferrin receptor positive cells are unstimulated B lymphocytes. **These studies provide the first documentation that constant infusion gallium treatment results in significant interference with iron metabolism and evidence for tissue iron depletion in vivo. These changes may correlate with therapeutic effects of gallium such as tumor response.**

Following is a study showing that gallium inhibits tumor growth in lung cancer. Besides demonstrating that smokers or ex-smokers would be wise to drink green tea, it offers a suggestion that gallium may be an antagonist of cadmium, which is probably the key toxic metal which is responsible for lung cancer.

Title

Magnesium alterations and pharmacokinetic data in *gallium*-treated lung cancer patients.

Author

Collery P; Millart H; Lamiable D; Vistelle R; Berthier A; Betbeze P; Cossart C; Mulette T; Masure F; Gourdier B; et al

Address

Centre Hospitalier Universitaire de Reims, France.

Source

Magnesium, 8(1):56-64 1989

Abstract

The dose of *gallium* chloride required to inhibit tumor growth after oral and chronic administration depends on the stage of the cancer disease and of the type of metastases. A dose regimen of 800 mg/24 h of *gallium* chloride will provide serum *gallium* concentrations greater than or equal to 600 micrograms/l in lung cancer patients with a small and limited disease. A dose of 1,400 mg/24 h is well tolerated in metastatic patients but may not be high enough to reach the desired serum *gallium* concentrations especially in patients with bone metastases. Radiotherapy and/or a chemotherapy will permit one to increase the serum *gallium* concentrations and the tumor *gallium* uptake by reducing the volume of the tumor. After chronic, oral administration of *gallium* a decrease in RBC Mg is noted. To avoid the Mg deficiency, the treatment must not be interrupted and may perhaps be decreased with care and slowly without resulting in a decrease of the serum *gallium* concentrations provided the treatment has been prolonged over a sufficient time to enable one to induce intratumor biological modifications and a decrease in the number of the malignant cells. Acute pharmacokinetic data are related to the histologic type of the tumor and may not be used to predict the serum gallium concentrations after chronic administration. The serum *gallium* concentrations required to inhibit the tumor growth may be higher in small cell lung carcinomas than in nonsmall cell lung carcinomas. Frequent Mg and Ga blood determinations are necessary to manage effective *gallium* treatment.

The following study indicates that gallium at 96 mgs per kilogram of body weight does not cause adverse effects. Based on this information I took 1/2 mg for my body weight of 100 kgs. I noticed an effect and feel that this is too much. However, it is possible that I was iron-deficient at the time and the negative effect of the gallium was due to a further depletion of iron. If you ever think about taking a gallium supplement, talk to me first.

Title

Evaluation of the reproductive toxicity of *gallium* nitrate in mice.

Author

Colomina MT; Llobet JM; Sirvent JJ; Domingo JL; Corbella J

Address

Laboratory of Toxicology and Biochemistry, School of Medicine, Rovira i Virgili, University, Reus, Spain.

Source

Food Chem Toxicol, 31(11):847-51 1993 Nov

Abstract

Reproduction studies were performed with *gallium* nitrate, an antihypercalcaemic drug that is also used as a chemotherapeutic agent for the

treatment of certain malignancies. Male mice were injected subcutaneously with **gallium** nitrate at doses of 0 (controls), 24, 48 and 96 mg/kg/day every other day for 14 days before mating with untreated females. Fertility and reproductive performance in the **gallium** nitrate-treated groups did not differ significantly from controls. No significant changes were observed in the relative testes and epididymis weights. Sperm counts in the **gallium** nitrate-dosed groups were comparable with those in the control group, whereas the percentage of motile cells was similar between treated and untreated animals. Histopathological examination of the testes and epididymis did not reveal any changes at any dose of **gallium** nitrate. **The no-observed-adverse effect level was 96 mg/kg body weight. This dose is about 30 times higher than the current doses of gallium nitrate administered to humans.**

The following toxicity study on gallium shows that, "

Title

Developmental toxicity evaluation of **gallium** nitrate in mice.

Author

G'omez M; S'anchez DJ; Domingo JL; Corbella J

Address

Laboratory of Toxicology and Biochemistry, School of Medicine, University of Barcelona, Reus, Spain.

Source

Arch Toxicol, 66(3):188-92 1992

Abstract

Gallium nitrate, a drug with antitumor activity, is presently undergoing clinical trials as a chemotherapeutic agent for the treatment of certain malignancies. Since there are very limited published animal toxicity data available, this study was conducted to investigate the potential adverse developmental effects of this drug. Pregnant Swiss mice were administered intraperitoneally **gallium** nitrate at 12.5, 25, 50, and 100 mg/kg/day on days 6, 8, 10, 12, and 14 of gestation. Monitors for maternal toxicity were body weight, food consumption and clinical signs. At sacrifice (day 18) maternal weight, liver and kidney weights, and gravid uterine weights were measured. Gestational parameters monitored were numbers of total implants, resorptions, postimplantation losses, and dead fetuses. Live fetuses were sexed, weighted, and examined for external, internal and skeletal malformations and variations. Maternal toxicity was noted in all the **gallium** nitrate-treated groups. Embryo/fetal toxicity was evidenced by a decrease in the number of viable implants, a reduction in fetal weight, and an increase in the number of skeletal variations (12.5, 25, 50 and 100 mg/kg). No significant increase in the incidence of malformations was observed at 12.5, 25, or 50 mg/kg. **The no-observable-adverse-effect level (NOAEL) for both maternal and developmental toxicity of gallium nitrate was less than 12.5 mg/kg.**

The following study shows that gallium preferentially binds to mucopolysaccharides. These are the proteins which are involved in the retro-ocular fibroblast proliferation found in ophthalmopathy (TED) and in pre-tibial myxedema.

Title

⁶⁷Ga-binding substances in stomach, small intestine, pancreas, and muscle.

Author

Ando A; Ando I; Hiraki T; Hisada K

Source

Eur J Nucl Med, 11(6-7):235-9 1985

Abstract

Normal male rats were injected with either **gallium** citrate Ga 67 or sodium sulfate S 35. After 24 h, the stomach, small intestine, pancreas, and muscle were excised and homogenized. After the removal of the nuclear fraction, each of these homogenates was digested with protease. After digestion, the supernatants of the reaction mixtures were applied to a Sephadex-G-100 column. The radioactivity was eluted with buffer solution. The resultant eluates were analyzed for radioactivity and the levels of proteins, uronic acids, and sialic acids. In all four organs, **sizable amounts of ⁶⁷Ga were bound to sulfated acid mucopolysaccharides with molecular masses of about 10,000 daltons and to sulfated acid mucopolysaccharides, a species whose molecular masses exceed 40,000 daltons.** In the stomach, large amounts of ⁶⁷Ga were bound to sulfated acid mucopolysaccharides with molecular masses of about 10,000 daltons. From these results, it is obvious that the main ⁶⁷Ga-binding substances in these four organs are sulfated acid mucopolysaccharides, and that these acid mucopolysaccharides play the most important role in the concentration of ⁶⁷Ga in these organs.

The following study shows that the binding location for gallium in tumor cells and inflammatory tissues is the mucopolysaccharide, heparin sulfate. The significance of this is unknown to me at this time but it looks like it may be important in light of the fact of sulfur's important role in thyroid disease.

Title

Involvement of heparan sulfate in ⁶⁷Ga binding to rat-liver plasma membrane.

Author

Kojima S; Kubodera A

Source

Eur J Nucl Med, 10(11-12):535-9 1985

Abstract

The role of heparan sulfate (HS) in **gallium** citrate Ga 67 binding to rat-liver plasma membrane was investigated. HS was found to be the only acid mucopolysaccharide present on the plasma-membrane surface. The extent of ⁶⁷Ga binding to the plasma membrane reached a plateau 1-2 h after the start of incubation, and binding was higher under alkaline conditions than under acidic conditions. The amount of binding increased in parallel with the protein concentration of the plasma membrane (up to 2 mg per incubation mixture). Solubilizing agents, such as bromelain and 1% Triton X-100 as well as 2 M NaCl and heparin, markedly decreased ⁶⁷Ga binding, and the decrease in ⁶⁷Ga binding to the plasma membrane was closely associated with the amount of HS released from the plasma-membrane surface by each solubilizing agent. On the other hand, treatment with HS markedly increased ⁶⁷Ga binding to about three times the control level. **These data provide further support for our previous proposal that HS plays an important role as a receptor for gallium in various tissues, including tumor cells and inflammatory tissues.**

The following study shows that gallium is effective in suppressing autoimmune disease. Uveitis is an inflammation of part or all of the uvea, the middle (vascular) tunic of the eye.

Title

Effect of **gallium** nitrate on experimental autoimmune uveitis.

Author

Lobanoff MC; Kozhich AT; Mullet DI; Gerber N; Gery I; Chan CC; Whitcup SM

Address

National Eye Institute, National Institutes of Health, Bethesda, MD 20892-1858, USA.

Source

Exp Eye Res, 65(6):797-801 1997 Dec

Abstract

Gallium nitrate (GN) has been shown to inhibit T cell-mediated inflammatory disease. The purpose of our study was to test the effect of *gallium* nitrate (GN) on experimental autoimmune uveitis (EAU). Experimental autoimmune uveitis was induced in male Lewis rats immunized with retinal S-antigen. Rats received subcutaneous injections of GN or saline one day prior to immunization and 1, 4, 7, 10, 13, 16, and 19 days after immunization. Ocular inflammation was graded clinically and histologically by masked observers, and in vitro assays of cell-mediated and humoral immunity were performed. GN significantly inhibited the development of EAU graded clinically ($P = 0.001$) and histologically ($P = 0.002$). Treatment with GN also resulted in a small (30-41%) decrease in the lymphocyte responses to retinal S-Antigen and a small (12-37%) reduction in antibody production to S-antigen. **These data show that GN suppresses the development of EAU, and inhibits both lymphocyte proliferative responses to antigen and antibody production.**

The following study suggests that gallium may inhibit the production of IgG antibodies. These are the antibodies believed to trigger hyperthyroidism in Graves' disease. However, the gallium was combined with arsenic, so the results are difficult to interpret.

Title

Immunotoxicity of the semiconductor *gallium* arsenide in female B6C3F1 mice.

Author

Sikorski EE; McCay JA; White KL Jr; Bradley SG; Munson AE

Address

Department of Pharmacology, Medical College of Virginia, Virginia Commonwealth University, Richmond 23298.

Source

Fundam Appl Toxicol, 13(4):843-58 1989 Nov

Abstract

The effects of *gallium* arsenide (GaAs) exposure on immunocompetence of B6C3F1 female mice were investigated. GaAs was administered as a single intratracheal instillation at doses of 50, 100, and 200 mg/kg. Fourteen days after exposure, various cellular and humoral immune parameters were assessed. GaAs exposure increased spleen cellularity in a dose-dependent manner. However, the percentages of Thy 1.2 positive and Ig positive cells were decreased and that of F4/80 positive cells was increased dose dependently. **The IgM and IgG antibody-forming cell response of the spleen to the T-dependent antigen sheep erythrocytes was reduced by 66 and 48%, respectively, at 200 mg/kg.** Levels of the serum complement protein, C3, were increased by as much as 16% with no significant change in CH50 levels. The mitogenic response of splenic T cells to Con A and PHA was unaffected by GaAs, but that of B cells to LPS was increased by 52%. The delayed hypersensitivity response to keyhole limpet hemocyanin and mixed lymphocyte response were significantly reduced in a dose-dependent manner by GaAs exposure. Natural killer cell activity against the YAC-1 mouse lymphoma was enhanced in treated mice. Analysis of peritoneal exudate cells (PEC) revealed a dose-dependent decrease in number and a shift in the composition of PECs. The percentage of PEC monocytes increased from 53% of the population to 81%, while the lymphocytes decreased from 46 to 20%. The adherent PEC population demonstrated decreased phagocytosis of covaspheres and increased phagocytosis of chicken erythrocytes (CRBC). GaAs exposure had no effect on host resistance to *Plasmodium yoelii* or *Streptococcus pneumoniae*, but dose dependently increased resistance of the mouse to *Listeria monocytogenes*. Treated mice demonstrated a significantly decreased resistance to the B16F10 melanoma with a sevenfold increase in tumor burden at 200 mg/kg. GaAs affects both humoral and cellular immune parameters in mice and impairs the ability of the immune system to protect against B16F10 tumor challenge.

In the following study gallium was shown to suppress the autoimmune disease lupus in mice, but the amount of gallium used was high.

Title

Gallium nitrate suppresses lupus in MRL/lpr mice.

Author

Apseloff G; Hackshaw KV; Whitacre C; Weisbrode SE; Gerber N

Address

Department of Pharmacology, College of Medicine, The Ohio State University, Columbus 43210-1239, USA.

Source

Naunyn Schmiedebergs Arch Pharmacol, 356(4):517-25 1997 Oct

Abstract

Gallium (Ga) nitrate, a drug which prevents a variety of experimental autoimmune diseases, was investigated in a murine model of systemic lupus erythematosus (SLE). In one experiment, female MRL/Mp lpr/lpr (MRL/lpr) mice were randomized into 2 groups of 6: 1) vehicle (trisodium citrate) and 2) Ga. Subcutaneous injections began at 3 weeks of age and continued weekly until the mice were euthanized a week after the thirteenth injection. The loading dose of Ga (calculated as elemental Ga) was 45 mg/kg, followed by 15 mg/kg/week. In another experiment ($n = 18$) with 3 males and 3 females per group, mice received 1) vehicle, 2) Ga x 1 (one 45 mg/kg dose), and 3) Ga x 13. In the experiment with 12 mice, axillary lymph nodes from Ga-treated mice were significantly smaller than those from vehicle-treated mice (91 ± 42 and 360 ± 358 mg respectively, mean \pm SD), and spleens as well as lymph nodes from the former showed significantly less lymphoid infiltrate. In the experiment with 18 mice, prescapular lymph nodes weighed 312 ± 98 , 217 ± 52 , and 42 ± 34 mg, and spleens weighed 732 ± 492 , 409 ± 164 , and 192 ± 93 mg in the groups which received vehicle, Ga x 1, and Ga x 13 respectively. Control mice had significantly more lymphoid infiltrates in the lungs, spleen, and lymph nodes and, unlike Ga x 13 mice, exhibited glomerulitis and renal vasculitis. **Within groups, females developed more severe disease than males.** The Ga x 13 group had increased percentages of CD4-bearing and CD8-bearing lymphocytes in lymph nodes and increased CD4-bearing lymphocytes in the spleen, with an increased proliferative response to mitogen stimulation in vitro in lymph nodes, although not in the spleen. The Ga x 13 group also gained less weight and developed osteosclerosis. Although preliminary, our findings suggest that clinical trials with Ga in SLE are merited.

The following study shows a significant gallium accumulation in the orbits and parotid glands of a patient with Sjogren's syndrome, a disease which appears related to Graves' disease and which seems to involve disturbances of copper metabolism.

Title

Subclinical Sjögren's syndrome: a significant ⁶⁷gallium accumulation in the orbits and parotid glands.

Author

Tanaka H; Onodera N; Ito R; Higuchi A; Suzuki Y; Monma N; Waga S

Address

Division of Pediatrics, Iwate Prefectural Kitakami Hospital, Japan.

Source

Acta Paediatr Jpn, 40(6):621-3 1998 Dec

Abstract

An 8-year-old girl with hypergammaglobulinemia showed an abnormal ⁶⁷gallium accumulation in the orbits and parotid glands.

Although she did not have any subjective siccant complaints, reported typical histopathological and sialographic changes suggesting Sjögren's syndrome (SjS) were observed in the salivary glands. *Gallium* scintigram might be a valuable and non-invasive diagnostic tool in the diagnosis of children with SjS without sicca symptoms.

The following study indicates that one of the mechanisms by which gallium helps autoimmune disease is by inhibiting T-cell activation.

Title

Modulation of in vitro and in vivo T-cell responses by transferrin-*gallium* and *gallium* nitrate.

Author

Drobyski WR; Ul-Haq R; Majewski D; Chitambar CR

Address

Division of Hematology/Oncology, Medical College of Wisconsin, Milwaukee, USA.

Source

Blood, 88(8):3056-64 1996 Oct 15

Abstract

Gallium is a group IIIa metal that has efficacy in the therapy of malignant disorders such as lymphoma and urothelial tract tumors. **Preclinical studies also indicate a role for gallium in autoimmune disorders, suggesting that gallium is able to modulate T-cell immune reactivity.** The purpose of this study was to examine the in vitro and in vivo immunomodulatory action of *gallium* on T-cell function. Since *gallium* binds to transferrin in vivo, in vitro studies evaluated the effect of transferrin-*gallium* (Tf-Ga) on human T cells. Tf-Ga inhibited the mitogen-induced proliferative response of peripheral blood mononuclear cells (PBMC) in a dose-dependent fashion. Alloantigen-induced proliferation was also potentially suppressed when evaluated in a mixed lymphocyte culture assay. Tf-Ga affected a significant reduction in the density of IL-2 receptors on activated T cells and a slight reduction in the number of CD3+/CD25+ T cells in PHA-stimulated cultures. Neither secretion of interleukin-2 (IL-2) nor the induction of IL-2-stimulated lymphokine-activated killer activity, however, was inhibited by Tf-Ga. Tf-Ga produced significant upregulation of the transferrin receptor (CD71) in T cells as determined by flow cytometric analysis and northern blot assay, but did not affect the percentage of CD3+/CD71+ T cells after mitogen stimulation. To assess the in vivo effects of *gallium* on alloreactive T cells, we evaluated the immunosuppressive effect of *gallium* in a murine model of graft-versus-host disease (GVHD). Administration of *gallium* significantly prolonged survival in mice undergoing severe GVHD, suggesting that *gallium* can ameliorate GVH reactivity. **Collectively, these data demonstrate that, at clinically achievable concentrations, Tf-Ga potently inhibits T-cell activation and that this immunosuppressive property of gallium may be of adjunctive therapeutic value in the management of disorders characterized by the presence of autoreactive or alloreactive T-cell populations.**

The conclusion of the following study is that the mechanism by which gallium accumulates in inflammatory tissue is its binding to the acid mucopolysaccharide present in the tissue.

Title

Mechanism of *gallium* ⁶⁷ accumulation in inflammatory tissue.

Author

Ando A; Nitta K; Ando I; Sanada S; Katsuda S; Tonami N; Hiraki T; Hisada K; Ogawa H

Address

School of Allied Medical Professions, Kanazawa University, Japan.

Source

Eur J Nucl Med, 17(1-2):21-7 1990

Abstract

The present study was undertaken to elucidate the accumulation mechanism of gallium ⁶⁷ in inflammatory tissue. ⁶⁷Ga accumulation in inflammatory tissue was observed by macro- and microautoradiogram. Permeability indices were calculated for serum albumin from blood vessels into inflammatory and normal tissue. Neutrophils and macrophages did not play a major role in ⁶⁷Ga accumulation in the inflammatory tissue because ⁶⁷Ga could hardly be detected in the sites in which neutrophils were crowded; the accumulation was concentrated in the intercellular space around these cells in the tissue. Permeability indices for inflammatory tissue were much greater than those for normal tissues. **It is thought from the present study and previously reported results that ⁶⁷Ga, together with plasma from permeable blood vessels, readily penetrates the inflammatory tissue and stays there by binding to the acid mucopolysaccharide present in the tissue.**

The following study shows that both gallium and iron have a high affinity for the acid mucopolysaccharide heparin sulfate. Also it was shown that high zinc intake caused an increase in the gallium uptake into the liver and a decrease in the iron uptake. Thus high zinc might interfere with the iron binding to heparin sulfate and this increases the availability of heparin sulfate to bind to gallium.

Title

Relation between ⁶⁷Ga uptake and iron metabolism in rat tissues.

Author

Kojima S; Sasaki T; Kubodera A

Source

Eur J Nucl Med, 9(1):33-8 1984

Abstract

The relationship between ^{67}Ga uptake and iron metabolism was investigated in rat tissues. **^{67}Ga and $^{59}\text{Fe(II)}$ both accumulated in the mitochondrial-lysosomal fraction after being injected. Moreover, they both showed especially high affinity for heparan sulfate (HS) among various acid mucopolysaccharides (AMPS).** When iron (ferrous citrate) was injected IV before, simultaneously with, and after ^{67}Ga citrate IV injection, ^{67}Ga uptake was significantly inhibited in normal rat liver in all cases. Elevated ^{67}Ga uptake in the liver of CCl_4 -treated rats was also lowered to the control level by iron pretreatment. **High zinc intake remarkably elevated the ^{67}Ga uptake in rat liver. The contents of iron in the liver and liver AMPS of 0.75% zinc-fed rats were lowered in comparison with those in controls. Thus, the elevation of ^{67}Ga uptake in the liver of zinc-fed rats might be due to the decrease of iron bound to HS.**

The following study shows that gallium also binds to the mucopolysaccharide keratin sulfate. Keratin is the structural component of the fingernails, hair, and cornea, all areas that become weak in Graves' hyperthyroidism.

Title

Species of ^{67}Ga -binding acid mucopolysaccharide in liver.

Author

Ando A; Ando I

Source

Int J Nucl Med Biol, 12(5):357-62 1985

Abstract

It was determined from measuring neutral saccharide in the structure that the principal ^{67}Ga -binding acid mucopolysaccharide in liver was keratan sulfate and/or keratan polysulfate. On the other hand, it was clarified from the results of mucopolysaccharase treatment that the main ^{67}Ga -binding acid mucopolysaccharide in liver was not either one of keratan sulfate, heparan sulfate, heparin, chondroitin sulfate A, B and C. Based on the present results, it was deduced that the main ^{67}Ga -binding acid mucopolysaccharide in liver was keratan polysulfate.

The following study shows that gallium is preferentially accumulated in the inflammation cells of interstitial lung disease associated with sclerosis. This may be more evidence that a gallium deficiency is involved with inflammation processes such as we see in ophthalmopathy.

Title

Evidence for chronic inflammation as a component of the interstitial lung disease associated with progressive systemic sclerosis.

Author

Rossi GA; Bitterman PB; Rennard SI; Ferrans VJ; Crystal RG

Source

Am Rev Respir Dis, 131(4):612-7 1985 Apr

Abstract

Progressive systemic sclerosis (PSS) is a generalized disorder characterized by fibrosis of many organs including the lung parenchyma. Unlike most other interstitial disorders, traditional concepts of the interstitial lung disease associated with PSS have held it to be a "pure fibrotic disorder without a significant inflammatory component. To directly evaluate whether an active alveolitis is associated with this disorder, patients with chronic interstitial lung disease and PSS were studied by open lung biopsy, ***gallium-67*** scanning, and bronchoalveolar lavage. Histologic evaluation of the biopsies demonstrated that the interstitial fibrosis of PSS is clearly associated with the presence of macrophages, lymphocytes, and polymorphonuclear leukocytes, both in the interstitium and on the alveolar epithelial surface. **Gallium-67 scans were positive in 77% of the patients, showing diffuse, primarily lower zone uptake, suggestive of active inflammation.** Consistent with the histologic findings, bronchoalveolar lavage studies demonstrated a mild increase in the proportions of neutrophils and eosinophils with occasional increased numbers of lymphocytes. Importantly, alveolar macrophages from patients with PSS showed increased release of fibronectin and alveolar-macrophage-derived growth factor, mediators that together stimulate lung fibroblasts to proliferate, thus suggesting at least one mechanism modulating the lung fibrosis of these patients. Thus, evidence from several different points of view together demonstrates that the interstitial lung disease associated with PSS is associated with chronic inflammation in the local milieu, leading to the hypothesis that the inflammation plays some role in the derangements to the alveolar structures that characterize this disorder.(ABSTRACT TRUNCATED AT 250 WORDS)

The following study suggests that a gallium deficiency might be involved in Alzheimer's disease and Down syndrome. High aluminum is found in the brain in these diseases and since aluminum is directly above gallium in the Periodic Table, this suggests that a gallium deficiency allows the aluminum to accumulate. Another interpretation is that excessive iron binds to the transferrin depriving gallium from being transported by transferrin. This resultant lack of gallium allows aluminum to build up in the cells. Perhaps the disturbance starts with a copper deficiency which allows the iron to build up and occupy a dominate share of the transferrin binding sites.

Lancet 1990 Mar 31;335(8692):747-50

Defective gallium-transferrin binding in Alzheimer disease and Down syndrome: possible mechanism for accumulation of aluminum in brain.

Farrar G, Altmann P, Welch S, Wychrij O, Ghose B, Lejeune J, Corbett J, Prasher V, Blair JA

Division of Biology, University of Aston, Birmingham, UK.

The plasma distribution of gallium (as an analogue of aluminium) was investigated in patients with Alzheimer disease, Down syndrome, or stroke dementia, in subjects on haemodialysis for chronic renal failure, and in healthy controls. **Gallium-transferrin binding was significantly lower in the Alzheimer (mean [SEM] 7.9 [1.1]%) and Down syndrome groups (6.9 [0.7]%) than in the controls (17.1 [1.6]%),** whereas stroke dementia and haemodialysis patients had normal binding. There were no differences among the groups in plasma citrate concentration. The plasma transferrin concentration was slightly lower in the Alzheimer and Down syndrome groups than in the controls, but even lower in stroke dementia patients (1.74 [0.14] g/l vs 2.98 [0.18] g/l in controls). **Transferrin iron saturation was higher in the Alzheimer (58.9%)**

and Down syndrome groups (81.6%) than in the controls (39.0%) or stroke dementia patients (33.4%). This deficiency of gallium/aluminium binding would leave more unbound aluminium which could move readily into the brain, where it has neurotoxic effects.

The following is an interesting hypothesis that there is a connection between the metals found to make good semiconductors for computers and the metals which are found to have anti-tumor activity. I like the idea. Very thought provoking.

Med Hypotheses 1988 Aug;26(4):239-49

Carcinogenesis as the result of the deficiency of some essential trace elements.

Marczynski B

Department of Biochemistry, Silesian University, Katowice, Poland.

"Energetic" biological trace elements [gallium (III), germanium (IV), silicon (silica), arsenic (V) and selenium (IV)] occurring in DNA of eukaryotic cells may improve the semiconductor properties of DNA and may influence the mechanisms that control genetic expression at the electronic level. Their roles are postulated as follows: (i) to maintain the level and direction of free sliding electrons in DNA, (ii) to modulate the electron conductivity and hole conductivity of DNA. This specific electronic nature of DNA take the form of magnetic pigeonholes in which an electric pulse is (0), or is not (1) stored as an area of local magnetisation. These types of conductivity occurring in different parts of DNA of different cells could participate in the switch on and switch off of genetic information in gene expression. This model may help to elucidate the mechanism of action of these naturally occurring antitumor agents and may help in understanding the role of trace elements in charge transport of DNA and in carcinogenesis.

Following is an interesting study showing an increase accumulation of gallium in the lungs of patients with AIDS. Is a gallium deficiency involved in AIDS?

J Nucl Med 1987 Dec;28(12):1915-9

Gallium scanning in lymphoid interstitial pneumonitis of children with AIDS.

Schiff RG, Kabat L, Kamani N

Department of Radiology, Schneider Children's Hospital, New Hyde Park, New York.

Lymphoid interstitial pneumonitis (LIP) is a frequent pulmonary complication in the child with the acquired immune deficiency syndrome (AIDS) and human immunodeficiency virus (HIV) infection. We report the gallium scan findings in two children with AIDS and LIP. Gallium scintigraphy in both children demonstrated increased radionuclide concentration throughout the lungs, a pattern indistinguishable scintigraphically from that of *Pneumocystis carinii* pneumonia (PCP). This should alert nuclear medicine practitioners and referring physicians to another cause of diffusely increased gallium uptake in the lungs of patients with AIDS.

Another study indicating that intense gallium uptake by the thyroid is a characteristic of hyperthyroidism.

Gallium-avid painless thyroiditis in a patient with AIDS.

Achong DM, Snow KJ

Department of Radiology, New England Medical Center, Boston, Massachusetts 02111.

Intense thyroidal Ga-67 accumulation was seen in a man with AIDS imaged for suspected *Pneumocystis carinii* pneumonia. Concurrent Tc-99m pertechnetate thyroid scanning demonstrated absent trapping, helping establish the diagnosis of painless thyroiditis. Occult hyperthyroidism, and not pulmonary infection, may have been responsible for the patient's original presenting symptoms.

Another study linking uptake of gallium with thymus disease.

Thymic hyperplasia associated with Hodgkin disease and thyrotoxicosis.

Pendlebury SC, Boyages S, Koutts J, Boyages J

Joint Lymphoma Clinic, Westmead Hospital, New South Wales, Australia.

A 19-year-old woman had a residual gallium-sequestering mediastinal mass after treatment for Hodgkin disease. Coincidentally, she also had hyperthyroidism. The initial concern was that the mass was residual Hodgkin disease. Thymic hyperplasia has been described in association with both these conditions. The mass disappeared after treatment of her hyperthyroidism.

Cancer Chemother Rep 1975 May-Jun;59(3):599-610

Another study showing the power of gallium to suppress cancer. If you ever get cancer, think of gallium first. Meanwhile drink green tea.

Studies on the antitumor activity of gallium nitrate (NSC-15200) and other group IIIa metal salts.

Adamson RH, Canellos GP, Sieber SM

Several group IIIa metal salts, eg, aluminum nitrate, gallium nitrate, indium nitrate, and thallium chloride, have been evaluated for in vivo toxicity in mice and rats, for cytotoxicity in tumor cells in vitro, and for activity against a broad spectrum of experimental rodent tumors. The position of these agents in the periodical table roughly parallels their toxicity, the LD50s decreasing with increasing atomic weights. This

parallel also exists with regard to in vitro cytotoxicity to Walker 256 carcinosarcoma cells. Although all of the metal salts had activity against the ascites Walker 256 carcinosarcoma, they were ineffective in ascites leukemias, plasma cell tumors, or Ehrlich carcinoma. **Gallium nitrate was particularly active against solid tumors transplanted subcutaneously, suppressing the growth of six of eight tumors more than 90%. Because of its demonstrated antitumor activity in rodents and its uptake and concentration by various animal and human tumors, gallium nitrate has potential usefulness in the treatment of solid tumors in man and has been entered into a phase I study at the National Cancer Institute.**

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Is the RAIU test a good idea?

It seems that every doctor tries to get their thyroid patients to undergo this test in which a "small" amount of radioactive iodine is ingested and the uptake of iodine into the thyroid can be measured.

One member of our group reported that she developed vision problems right after this test. Upon going to an ophthalmologist, it was determined that she had macular degeneration and was legally blind in one eye. The macula is the central area of the eye's retina critical to vision.

I looked into this situation and found sufficient information to make me believe that the radioactive iodine might go to the macula and cause damage there. I found a study in which patients with macular degeneration were given iodine (non-radioactive) and this resulted in a significant improvement in their vision, especially their color vision. This indicates that macular degeneration may involve an iodine deficiency.

If iodine is indeed involved in ocular functions, then radioactive iodine would replace some of the normal iodine there. When the radioactive iodine breaks down, cellular damage from the radioactivity can occur. Also, it's possible as the radioactive iodine breaks down, the iodine is transformed into an element with a lower atomic weight. This means that the normal iodine which is supposed to be there has now been replaced by another element. I would suspect that this would be a problem but more information is needed.

I think it's possible that the RAIU test may damage the vision and am looking into this. In the meantime, I can't see any reason for undergoing this test. Doctors use this test to determine how much radioactive iodine to give the patient in RAI. If you're not going to get RAI, are the results of this test important? How are the results going to influence your treatment? I don't see any benefit.

The RAI-Uptake Test and Scan by Elaine Moore September 3, 2000

Patients who are initially diagnosed with hyperthyroidism are often ordered to have a radioiodine uptake test (RAI-U) or scan. The idea here is that true hyperthyroidism can be distinguished from conditions where patients happen to be taking excess thyroid hormone or have transient thyroiditis due to infections.

Most importantly, the docs want to know if the patient has Graves' disease, or autoimmune hyperthyroidism, which is responsible for more than 90% of all cases of hyperthyroidism in the West. Why is the RAI-U no longer needed? A blood test for stimulating TSH receptor antibodies is more specific and it doesn't expose the patient and his or her already stressed thyroid to excess radioiodine.

Because the RAI-U is seldom properly explained, many hyperthyroid patients are confused and think they're receiving radioiodine ablation to destroy their thyroids. The RAI-U has a similar principle but a smaller amount of a different isotope is used for the diagnostic test. For ablation, I-131 is usually used, and for the RAI-U, I-125 is used.

For both the test and the ablative procedure, radioiodine is given orally as a dose or drink. In the test, however, the amount of radioiodine taken up by the thyroid gland is measured by an imaging test after any period of time from 2-24 hours. At the same time, a scan is done to show how the iodine is distributed throughout the gland. In Graves' disease, the uptake is high and the pattern of the scan is diffuse. In the case of nodules, there will be spots in the scan with differences in density.

The normal range for the RAI-U is 8% to 35% although the ranges are different in various geographic locations, relative to dietary iodine concentrations. Some researchers say that with the increased iodine content of the American diet, the RAI-U no longer shows clear abnormalities.

RAI-U is increased in hyperthyroidism, iodine deficiency, pregnancy, hydatidiform mole, recovery phase of subacute thyroiditis, rebound after TSH suppression, rebound phase after withdrawal of strong iodine solution or anti-thyroid drugs if the TSH is elevated, therapeutic lithium and inborn errors of thyroid hormonogenesis. From this list, it's clear that the RAI-U is not a specific test for diagnosing Graves' disease. In fact, in patients with T3 thyrotoxicosis, the value may be decreased. The test for stimulating TSH receptor antibodies or TSI is diagnostic for Graves' disease.

There are several sources of error for the RAI-U, most significantly iodine contrast dyes used in imaging studies. These may interfere with test results for several months. Excess dietary iodine in the form of kelp or as inorganic iodine in multivitamins also skews the results.

And according to John Gofman, a physician and doctor on nuclear/physical chemistry, the radioiodines in diagnostic procedures are just as hazardous as the radioiodine used as an ablative treatment. Gofman cautions that the effects of ionizing radiation on chromosomes in stem cells may take more than 30 years to emerge.

Most docs prefer the RAI-U test. After all it's done locally (often at the clinic at the doctor's office, generating revenue for the clinic) and results are generated quickly, compared to the blood test which usually needs to be sent to a national reference lab and takes several days for results. However, the blood test is superior for diagnosing

Graves' disease as well as a safer approach.

Following is my reply to a father whose 12 year-old daughter experienced a sudden decline in vision following a RAIU test. He wanted to know what to ask the ophthalmologist when he took his daughter to see him.

Hi,

It does sound like your daughter has Graves'/hyperthyroidism. Age 12-14 is the age when girls get it. When they start their periods, the extra blood loss can push the ones with marginal copper status over the edge into enough deficiency to cause hyperT. Doctors don't know anything about this and since they think they know everything they won't listen either. If you give her some copper she will probably recover pretty fast.

The RAIU--eyesight problem is very speculative at this point. But if the radioiodine did cause the problem, then there will probably be some indication of macular degeneration. Have the ophthalmologist check her for macular degeneration. I wouldn't say anything about suspecting radioiodine as the cause beforehand, but ask him afterward if there is any possible reason to suspect a connection. Generally doctors don't want to get into a situation where their diagnosis might suggest that another doctor is guilty of malpractice. They all work to protect each other like fraternity brothers.

Most likely you'll never know if there is a connection, but if we can collect enough cases where vision has suddenly deteriorated after RAIU, we might get someone to investigate a possible cause and effect relationship.

Ok--I just did a PubMed search and came up with some things. It looks like there is a condition called radiation retinopathy which is a deterioration of the central retina (probably the macula) following radiation treatment. There are thousands of studies about radiation retinopathy, so it must be a well known condition. I looked up radiation retinopathy and Graves and came up with some pertinent studies.

The first one below indicates that the radiation retinopathy was the result of an excess amount of radiation given to the patient. This suggests that you need to go back to the radiation lab and have someone other than the persons involved check to see if your daughter was mistakenly given more radiation than she was supposed to get.

Later down the page you'll see a study where patients with age-related macular degeneration recovered some visual acuity after ingesting (or bathing in) iodine water. This is why I suggested giving your daughter iodine for her eyes. You'll need copper first so the iodine doesn't aggravate the hyper symptoms.

So when you go to the ophthalmologist, ask if she has retinopathy. Then subsequently if the answer is yes or maybe, ask if it could be radiation retinopathy since it occurred right after a RAIU test. Also, we had another group member who had the RAIU test and had diminished vision right afterward to the point of being declared legally blind in one eye.

As I stated above, I really think there is some connection between the radiation and the vision problems observed right afterward. I hope we can get more evidence that the RAIU test is a possible cause. Best wishes, John

Arch Ophthalmol 1984 Oct;102(10):1473-6 Related Articles, Books, LinkOut

Radiation retinopathy after orbital irradiation for Graves' ophthalmopathy.

Kinyoun JL, Kalina RE, Brower SA, Mills RP, Johnson RH

Recent reports indicate that orbital irradiation for Graves' ophthalmopathy is sometimes beneficial, particularly for dysthyroid optic neuropathy, and is not associated with serious complications. We are aware, however, of four patients who were found to have radiation retinopathy after orbital irradiation for Grave's ophthalmopathy. All four patients have decreased central acuity, and three of the four are legally blind in one or both eyes. Computer reconstruction of the dosimetry, based on computed tomography and beam profiles, shows that errors in dosage calculations and radiotherapy technique probably account for the radiation retinopathy in three of the four patients. Radiotherapy for Graves' ophthalmopathy should be administered only by competent radiotherapists who are experienced in the treatment of this disease. Similar errors in dosage calculations and treatment techniques may account for other reports of radiation retinopathy after reportedly safe dosages.

Ophtalmologie 1990 May-Jun;4(3):229-31 Related Articles, Books, LinkOut

[Maculopathy caused by irradiation in patients treated for choroid melanoma].

[Article in French]

Haye C, Desjardins L, Boudier P, Schlienger P, Dorval T

Institut Curie, Paris.

We are using Cobalt 60 plaques at Curie Institute since 1968 for the treatment of malignant choroidal melanoma.

We reviewed a series of 79 patients treated between 1982 and 1984 with a minimal follow up of 5 years. Tumors thickness varies between 2 and 11 mm with a mean thickness of 5.7 mm. All the tumors received at least 70 grays at the apex. 7 patients died from other cause, 7 patients presented metastasis 65 patients are alive and well, 49 of them have kept their eye and 16 have been enucleated. 18 patients have a visual acuity below 20/200 because of severe maculopathy, 29 patients have a visual acuity between 20/200 and 20/25. The most severe functional visual loss was due to maculopathy. It consisted of obliteration of the capillaries, exsudation and cystoid macular oedema. If we compare these results to other authors we see that maculopathy is a frequent problem with cobalt 60. For these reasons, we intend in the future to use iodine 125 plaques and prothontherapie that should give us better functional results.

Arch Ophthalmol 1999 May;117(5):609-14 Related Articles, Books, LinkOut

Radiation retinopathy following plaque radiotherapy for posterior uveal melanoma.

Gunduz K, Shields CL, Shields JA, Cater J, Freire JE, Brady LW

Oncology Service, Wills Eye Hospital, Thomas Jefferson University, Philadelphia, PA 19107, USA.

OBJECTIVE: To identify the risk factors that lead to the development of radiation retinopathy following plaque radiotherapy for posterior uveal melanoma. Radiation retinopathy is a slowly progressive, occlusive vasculopathy characterized by radiation-induced endothelial damage. **METHODS:** Review of the medical records of patients with posterior uveal melanoma treated with plaque radiotherapy. **RESULTS:** Of 1300 patients with posterior uveal melanoma treated with plaque radiotherapy from July 1, 1976, through June 30, 1992, radiation retinopathy developed in 560 (43.1%). By using Kaplan-Meier survival estimates, we found that 5% of the patients had nonproliferative radiation retinopathy at 1 year (95% confidence interval [CI], 3%-6%) and 42% at 5 years (95% CI, 38%-45%). The proportion of patients with proliferative retinopathy was 1% at 1 year (95% CI, 0.2%-1.5%) and 8% at 5 years (95% CI, 5%-10%). Multivariate analyses showed that the subset of clinical variables best related to the development of nonproliferative radiation retinopathy were tumor margin of less than 4 mm from foveola ($P < .001$), tumor limited to the choroid ($P = .002$), and radiation dose rate of greater than 260 cGy/h to the tumor base ($P = .02$). The best subset of independent variables related to the development of radiation maculopathy were tumor of less than 4 mm to foveola ($P < .001$) and the use of radioisotope iridium 192 (^{192}Ir) ($P = .02$) compared with iodine 125 (^{125}I). From a multivariate model, the most important factors for the development of proliferative radiation retinopathy included diabetes mellitus ($P = .01$), radioisotope ^{192}Ir ($P = .01$) compared with ^{125}I , and tumor base of greater than 10 mm ($P = .02$). **CONCLUSIONS:** Radiation retinopathy is a common finding after plaque radiotherapy for choroidal melanoma, occurring in 42% of patients at 5 years. The main predictors of radiation retinopathy are posterior tumor location with margin near the foveola and high radiation dose rate to the tumor base.

Noble KG. Related Articles

Central retinal artery occlusion: the presenting sign in radiation retinopathy.
Arch Ophthalmol. 1994 Nov;112(11):1409-10. No abstract available.
PMID: 7980127

Miller ML, Goldberg SH, Bullock JD. Related Articles

Radiation retinopathy after standard radiotherapy for thyroid-related ophthalmopathy.
Am J Ophthalmol. 1991 Nov 15;112(5):600-1. No abstract available.
PMID: 1951605

Nikoskelainen E, Joensuu M. Related Articles

Retinopathy after irradiation for Graves' ophthalmopathy.
Lancet. 1989 Sep 16;2(8664):690-1. No abstract available.
PMID: 2570949

Ophthalmologica 1992;205(2):100-4 Related Articles, Books, LinkOut

[Changes in Contrast Sensitivity after Iodine Treatment in Bad Hall in Patients with Age-Related Maculopathy].

[Article in German]

Rieger G

Augenabteilung des Paracelsus- Institutes des Landes, Oberosterreich in Bad Hall.

After a cure with iodine in Bad Hall (Upper Austria), patients with age-related maculopathy repeatedly reported improvement in visual power: the picture seen seems to be clearer on the whole or more distinct. These statements were checked in 50 patients with beginning age-related macula degeneration ('dry form') using the 'Vision Contrast test system (VCTS 6500)'. The analysis of the results showed that there is indeed a statistically highly significant

improvement in contrast sensitivity after the cure ($p < 0.0001$). The spontaneous observations of the patients were therefore confirmed by the study.

PMID: 1475080

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GLUTATHIONE

Glutathione (GSH) is a tripeptide formed from glutamic acid, cysteine, and glycine. Combined with vitamin E and selenium, glutathione forms glutathione peroxidase (GPx) which is one of the key antioxidants that protects the body and is critical for protection of the thyroid gland from oxidation damage.

Low levels of glutathione (along with low levels of vitamin E and selenium) may be a factor in the genesis of thyroid disease. Excessive intake of sugars and starches may reduce glutathione and thereby damage the thyroid gland.

Title

Role of the hepatic xanthine oxidase in thyroid dysfunction: effect of thyroid hormones in oxidative stress in rat liver.

Author

Huh K; Kwon TH; Kim JS; Park JM

Address

Department of Pharmacology, College of Pharmacy, Yeungnam University, Gyongsan, Korea.

Source

Arch Pharm Res, 21(3):236-40 1998 Jun

Abstract

The effect of thyroid hormones on the hepatic xanthine oxidase activity was studied in rats after the intraperitoneal injections of comthyroid (triiodotyronine:thyroxine = 1:4) at 0.3 mg/kg for 3 consecutive days. The aim of this study was to understand the precise mechanism of hyperthyroidism induced by oxidative stress. The concentration of lipid peroxides determined indirectly by the measurement of thiobarbituric acid reactants was increased in comthyroid treated rats. The hepatic *glutathione* content was decreased in comthyroid injected rat compared to the euthyroid state. It was also observed that the increment of xanthine oxidase activity has a profound role in oxygen radicals generation system in comthyroid treated rat. These findings suggest that the enhanced xanthine oxidase activity and depleting *glutathione* content in comthyroid treated rats result in pathophysiological oxidative stress including an increment of hepatic lipid peroxidation.

Title

The effect of methimazole on the oxidant and antioxidant system in patients with hyperthyroidism.

Author

Ademoğlu E; Gökkuşu C; Yarman S; Azizlerli H

Address

Department of Biochemistry, Istanbul Faculty of Medicine, University of Istanbul, Turkey.

Source

Pharmacol Res, 38(2):93-6 1998 Aug

Abstract

The present study was designed to evaluate the changes in the plasma lipid peroxidation and antioxidant system in 15 adult volunteer patients in hyperthyroid and euthyroid states. In these patients, plasma concentrations of lipid peroxides were decreased and, ascorbic acid and vitamin E levels were significantly increased in euthyroid status in comparison to hyperthyroid status. A significant increase in the plasma GPx activity ($P < 0.01$) and a decrease in GST ($P < 0.001$) was observed after euthyroidism was sustained with methimazole therapy. In conclusion, hyperthyroidism tends to enhance lipid peroxide content and an increase in GST and decreases in GPx, vitamin E and ascorbic acid levels accompany to this change in the plasma. The achievement of euthyroidism led an improvement in these parameters.

This study shows that iron supplementation can increase the production of glutathione and glutathione peroxidase.

Title

The effect of iron supplementation on GSH levels, GSH-Px, and SOD activities of erythrocytes in L-thyroxine administration.

Author

Seymen O; Seven A; Candan G; Yigit G; Hatemi S; Hatemi H

Address

Department of Physiology, Cerrahpasa Medical Faculty, Istanbul University, Turkey.

Source

Acta Med Okayama, 51(3):129-33 1997 Jun

Abstract

Our aim was to study the effect of iron supplementation on the following aspects of erythrocyte metabolism in experimental hyperthyroidism: *glutathione* (GSH) levels, *glutathione* peroxidase (GSH-Px), and superoxide dismutase (SOD) activities. Hyperthyroidism induced by L-thyroxine administrations significantly raised erythrocyte GSH, GSH-Px and SOD levels of the rats ($P < 0.001$). Likewise, we observed that iron supplementation induced significant rises in erythrocyte GSH, GSH-Px and SOD levels ($P < 0.001$) as compared with the control group. The erythrocyte GSH, GSH-Px and SOD levels of hyperthyroidism-induced iron-supplemented animals were significantly higher when compared with either the iron-supplemented group ($P < 0.001$) or the only L-thyroxine-administered hyperthyroid group ($P < 0.001$, $P < 0.05$, $P < 0.01$, respectively). The results of this study show that L-thyroxine administration and/or iron supplementation increases GSH, GSH-Px and SOD levels of erythrocytes.

Title

Copper-glutathione complexes under physiological conditions: structures in solution different from the solid state coordination.

Author

Pederson JZ; Steinkühler C; Weser U; Rotilio G

Address

Department of Biology, University of Rome Tor Vergata, Italy.

Source

Biomaterials, 9(1):3-9 1996 Jan

Abstract

The physiologically important copper complexes of oxidized glutathione have been examined by electron spin resonance (ESR) spectroscopy in aqueous solution at neutral pH. Low temperature measurements show that the Cu(II) binding site in oxidized glutathione has the same ligand arrangement as in copper complexes of S-methylglutathione, *glutamine*, glutamate and glycine. The site is composed of the amino nitrogens and the carboxyl oxygens of two gamma-glutamyl residues; there is no interaction with amide nitrogens, the sulphur bond or the glycyl carboxyl groups. At high metal to ligand ratios a binuclear species exists, in which each Cu(II) binds only to one gamma-glutamyl residue. The previously reported forbidden transition detected at $g = 4$ is due to non-specific aggregation and not to spin coupling of intramolecular sites. Liquid solution ESR spectra show the Cu(II)-glutathione complex has a lower mobility than the corresponding Cu(II)-S-methylglutathione species. From the degree of spectral anisotropy the complex with glutathione is calculated to exist as a dimer. These results demonstrate that the physiologically relevant complex between copper and oxidized glutathione in solution is completely different from the known solid state structure determined by crystallography.

Title

Role of cytosolic *copper*, metallothionein and glutathione in *copper* toxicity in rat hepatoma tissue culture cells.

Author

Steinebach OM; Wolterbeek HT

Address

Department of Radiochemistry, Delft University of Technology, The Netherlands.

Source

Toxicology, 92(1-3):75-90 1994 Sep 6

Abstract

Effects of metallothionein (MT) synthesis inhibiting compounds (actinomycin D, cycloheximide), MT synthesis stimulating compounds (dexamethasone, dibu-cAMP) and interfering metals (Cd, Zn) on *copper* accumulation were investigated in rat hepatoma tissue culture cells. *Copper*-metallothionein (Cu-MT) and MT-associated *copper* levels were determined to find a possible correlation between cytosolic *copper* concentrations and MT as a Cu-detoxifying protein. Further, intracellular non-MT associated *copper* levels and levels of GSH and SOD were determined. Cell viability was tested under all experimental conditions by measuring LDH-release, K⁺ uptake and total cell protein. Administration of dexamethasone and dibu-cAMP showed no effect on MT levels (compared with controls), and only a marginal effect on ⁶⁴Cu and total Cu accumulation. Administration of actinomycin D resulted in increased *copper* accumulation in the particulate fraction, possibly due to inhibition of *copper* secretion processes and/or protein synthesis. Presence of zinc had no effect on MT levels nor on total Cu and ⁶⁴Cu levels, in contrast with cadmium which drastically enhanced *copper* accumulation and MT levels in the cells. Cu/MT ratios varied from 1.0 +/- 0.3 to 3.3 +/- 1.2, which is far below the assumed maximum molar ratio of 8-12 mol Cu per mol MT. SOD levels appeared to be enhanced up to 2- or 3-fold in the presence of Cd²⁺, relative to control values. The role of GSH as Cu-intermediate in intracellular Cu distribution plus its role in *copper* defence mechanism(s) was tested by application of BSO, an inhibitor of GSH synthesis. It was found that BSO had no effect on intracellular MT level; it was found however that MT-bound *copper* levels were markedly decreased. The results presented support a model for *copper* metabolism in hepatoma tissue culture (HTC) cells, where Cu(I) is complexed by GSH immediately after entering the cell. GSH is capable of transferring *copper* to MT where it is stored. Depletion of GSH (by administration of Cd²⁺, actinomycin D, cycloheximide) almost instantaneously results in enhanced cellular toxicity. When also MT is depleted (by actinomycin D) non-MT associated, 'free' cytosolic Cu²⁺ is elevated, and HTC cells rapidly lose their resistance to *copper* toxicity, as also reflected in loss of cell viability (LDH, K⁺ and total cell protein).

Title

The role of *glutathione* in copper metabolism and toxicity.

Author

Freedman JH; Ciriolo MR; Peisach J

Address

Institute for Structural and Functional Studies, University City Science Center, Philadelphia, Pennsylvania 19140.

Source

J Biol Chem, 264(10):5598-605 1989 Apr 5

Abstract

Cellular copper metabolism and the mechanism of resistance to copper toxicity were investigated using a wild type hepatoma cell line (HAC) and a copper-resistant cell line (HAC600) that accumulates

copper and has a highly elevated level of metallothionein (MT). Of the enzymes involved in reactive oxygen metabolism, only glutathione peroxidase was elevated (3-4-fold) in resistant cells, suggestive of an increase in the cellular flux of hydrogen peroxide. A majority of the cytoplasmic copper (greater than 60%) was isolated from both cell lines as a GSH complex. Kinetic studies of ^{67}Cu uptake showed that GSH bound ^{67}Cu before the metal was complexed by MT. Depletion of cellular GSH with buthionine sulfoximine inhibited the incorporation of ^{67}Cu into MT by greater than 50%. These results support a model of copper metabolism in which the metal is complexed by GSH soon after entering the cell. The complexed metal is then transferred to MT where it is stored. This study also indicates that resistance to metal toxicity in copper-resistant hepatoma cells is due to increases in both cellular GSH and MT. Furthermore, it is suggested that elevated levels of GSH peroxidase allows cells to more efficiently accommodate an increased cellular hydrogen peroxide flux that may occur as a consequence of elevated levels of cytoplasmic copper.

J Endocrinol Invest 1993 Apr;16(4):265-70

Acute iodine ingestion increases intrathyroidal glutathione.

Allen EM

Department of Medicine, University of Maryland Medical School, Baltimore.

In genetically predisposed individuals, autoimmune lymphocytic thyroiditis (LT) is potentiated by excess dietary iodine (I). There have been data which suggest that oxidative stress may have a role in iodine-induced LT. These in vivo studies were undertaken to examine the effect of iodine on intrathyroidal levels of the potent antioxidant glutathione (GSH) and see if the thyroids of LT-prone BB/Wor rats have aberrant GSH responses after iodine-loading. LT-prone BB/Wor, non LT-prone BB/Wor and Wistar rats were randomized to receive either 0.05% I (as NaI) or tap water. Thyroid and liver homogenates were assayed individually for GSH. Following the administration of 0.05% iodine water overnight, all of the animals demonstrated a rise in intrathyroidal GSH regardless of LT-proneness. To determine whether this was a dose-dependent response, Wistar rats were randomized to receive tap, 0.0125%, 0.025%, 0.05%, or 0.075% I, overnight. Intrathyroidal GSH levels rose with increasing iodine concentrations peaking at 0.025% I. Hepatic GSH levels were unaltered by iodine treatment. Ten days of 0.05% I water did not result in any difference between the GSH levels of thyroids from treated and control rats. Frozen sections of the thyroids and livers from iodine-treated rats were compared to tap-water controls after staining with Mercury Orange for GSH and Schiff's reagent for evidence of lipid peroxidation. Iodine-treated thyroids had an apparent shift of GSH staining from the apical border to the cytoplasm. However, there was no Schiff's staining indicative of lipid peroxidation in the iodine-treated thyroids.

PMID: 7685786, UI: 93294146

Title

Hepatic *glutathione* biosynthetic capacity in hyperthyroid rats.

Author

Fernández V; Videla LA

Address

Departamento de Bioquímica, Facultad de Medicina, Universidad de Chile, Santiago-7, Chile.

Source

Toxicol Lett, 89(2):85-9 1996 Dec 16

Abstract

The influence of hyperthyroidism on the capacity of the liver to synthesize *glutathione* (GSH) was evaluated as a possible mechanism of depletion of the tripeptide. For this purpose, the effect of daily doses of 0.1 mg 3, 3',5-tri-iodothyronine (T3)/kg for 3 consecutive days on hepatic GSH biosynthetic capacity was assessed by a combined assay measuring gamma-glutamylcysteinyl synthase and GSH synthase simultaneously. T3 treatment induced a significant 56% depletion of liver GSH in parallel with an increase in the rate of GSH synthesis, the latter effect being completely abolished by L-buthionine sulfoximine. According to these data, the fractional rate of hepatic GSH turnover exhibited a 3.2-fold enhancement in hyperthyroid rats compared to control animals. It is concluded that the enhanced GSH utilization in the liver of hyperthyroid rats previously observed [Fernández et al., Endocrinology 129, 85-91, 1991], is accompanied by an increment in GSH synthesis that is insufficient to sustain the basal levels of the tripeptide observed in euthyroid animals, thus establishing a low steady-state content of GSH in the tissue.

Title

Glucose may induce cell death through a free radical-mediated mechanism.

Author

Donnini D; Zambito AM; Perrella G; Ambesi-Impiombato FS; Curcio F

Address

Dipartimento di Patologia e Medicina Sperimentale e Clinica, University of Udine Medical School, Italy.

Source

Biochem Biophys Res Commun, 219(2):412-7 1996 Feb 15

Abstract

It has been reported that glucose may autooxidize generating free radicals which have been hypothesized to induce important cellular abnormalities. To investigate the cell damage induced by glucose-dependent oxidative stress, the FRTL5 cell strain was incubated in 10 or 20 mM glucose, either alone or in the presence of *buthionine*-sulfoximine, a transition state inhibitor that blocks glutathione synthesis. We found indeed that *buthionine*-sulfoximine greatly inhibited glutathione production and increased malondialdehyde (a marker of oxidative cell damage) levels, especially in 20mM glucose. We also found that, when glutathione production was inhibited, 10mM glucose induced apoptosis and 20 mM glucose induced necrosis. These data show that the glucose-dependent cell damage is a

function of glutathione production. They also show that such glucose-dependent free radical production may be critical for determining cell damage, even for small variations as the ones we tested (from 10 to 20 mM glucose).

Following is an article from Dr. Mercola's website, mercola.com, which talks about how high blood sugar can decrease glutathione and increase malonaldehyde, which can damage the thyroid and pancreas.

Lowering Blood Sugar Raises Glutathione and Vitamin E Levels

In this study of patients with type 2 diabetes, blood levels of two vital nutrients - glutathione and vitamin E - were found to increase when glucose levels dropped and blood sugar became better controlled.

In addition, levels of both of these nutrients increased even further in patients who received four weeks of vitamin E supplementation.

Although most people know about vitamin E, glutathione is not quite so well-known. It is a peptide consisting of glutamic acid, cysteine, and glycine. It serves as a critical co-enzyme for many reactions in the body.

In addition to the increased glutathione and vitamin E levels, levels of malonaldehyde, a naturally occurring possible carcinogen, were reduced following the reduction of blood glucose levels. Malonaldehyde occurs as a natural metabolic byproduct of prostaglandin synthesis and as an end product of polyunsaturated lipid peroxidation. The CDC has reported that there was clear evidence of carcinogenic activity in rats administered malonaldehyde, particularly effecting the thyroid gland and pancreas.

Annals of Nutrition and Metabolism 2000; 44: 11-13

COMMENT: Glutathione is one of the most essential antioxidants. One can take supplements for it, but the only form that works is the reduced form and this is very difficult to absorb orally. It is much more cost effective to supplement with precursors or items like alpha lipoic acid that regenerates glutathione. It also has the ability to regenerate other antioxidants such as vitamins C and E. Red meat and organ meats are the best sources of alpha lipoic acid. Glutamine is also a useful nutrient that improves intestinal health and also serves as a direct precursor to glutathione, and some investigators believe it to be the rate-limiting nutrient for glutathione formation.

Some nutritional authorities recommend taking a form of cysteine known as N-acetyl-cysteine (NAC), but I would advise against using this supplement if you still have mercury amalgam fillings because it could interfere with the detoxification of the mercury. Personally I consume 300 mg of alpha lipoic acid and 5,000 mg of glutamine and 2,500 mg of vitamin C before I do my seven-mile run as I believe it will maximize the glutathione production to decrease the damage from the free radicals that I generate when I exercise. Controlling the damage from free radicals is one of the keys to slowing down the aging process.

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GOITROGENS

Goitrogens are foods which suppress thyroid function. In normals, goitrogens can induce hypothyroidism and goiter. In hypos, goitrogens can further depress thyroidal function and stimulate the growth of the thyroid (goiter).

In hyperthyroids, goitrogens may help suppress thyroidal function until normal thyroidal functioning can be restored. However, this may not be a good strategy. Goitrogens work by interfering with the thyroidal uptake of iodine. While many hypers try to limit thyroid output by iodine restriction, this strategy can backfire. Iodine restriction will cause the thyroid to increase in size (goiter) in an effort to filter more blood to get more iodine. When iodine is then re-introduced to the diet or accidentally ingested, the now larger thyroid gland has the capacity for greater thyroid hormone production.

I do not believe that iodine restriction is a good long-term method for controlling thyroid hormone production. Therefore the consumption of goitrogens is not a good strategy. It is better to increase copper metabolism by supplementation of copper and the assisting nutrients. Once copper is replenished and copper metabolism is working properly, the body will tolerate iodine without increasing thyroid hormone production.

Many goitrogens are generally members of the brassica family. These include:

Broccoli
Cauliflower
Brussel Sprouts
Cabbage
Mustard
Kale
Turnips
Rape seed (Canola Oil)

Other goitrogens include:

Soy
Pine nuts
Millet
Peanuts

Brassica family vegetables not only inhibit thyroid production, but they also inhibit cancer growth. We know that sulfur, copper, and iron work closely together and that excessive sulfur can deplete copper and/or iron. The following study mentions that excessive kale consumption will cause anemia in cattle. Generally anemia is the result of low iron and/or copper. Also, foods and drugs that cause anemia also reduce cancer growth, indicating that the brassica vegetables might reduce cancer by inducing anemia.

Because copper and iron are so important for thyroid function, I don't think that it is advisable to eat plants of the brassica family. We have seen that the primary pre-condition for the production of thyroid disease is the onset of anemia. Brassica vegetables, with their high sulfur content, may be foods which induce anemia and consequently thyroid disease. Don't consider this the final word on these vegetables, but we will continue to look at this possibility.

Food Chem Toxicol 1995 Jun;33(6):537-43

Bioactive organosulfur phytochemicals in Brassica oleracea vegetables--a review.

Stoewsand GS.

Department of Food Science and Technology, New York State Agricultural Experiment Station, Cornell University, Geneva 14456, USA.

Sulfur-containing phytochemicals of two different kinds are present in all Brassica oleracea (Cruciferae) vegetables (cabbage, broccoli, etc.). They are glucosinolates (previously called thioglucosides) and S-methyl cysteine sulfoxide. These compounds, which are derived in plant tissue by amino acid biosynthesis, show quite different toxicological effects and appear to possess anticarcinogenic properties. Glucosinolates have been extensively studied since the mid-nineteenth century. They are present in plant foods besides Brassica vegetables with especially high levels in a number of seed meals fed to livestock. About 100 different kinds of glucosinolates are known to exist in the plant kingdom, but only about 10 are present in Brassica. The first toxic effects of isothiocyanates and other hydrolytic products from glucosinolates that were identified were goitre and a general inhibition of iodine uptake by the thyroid. Numerous studies have indicated that the hydrolytic products of at least three glucosinolates, 4-methyl-sulfinylbutyl (glucoraphanin), 2-phenylethyl

(gluconasturtiin) and 3-indolylmethyl (glucobrassicin), have anticarcinogenic activity. Indole-3-carbinol, a metabolite of glucobrassicin, has shown inhibitory effects in studies of human breast and ovarian cancers. Kale poisoning, or a severe haemolytic anaemia, was discovered in cattle in Europe in the 1930s, but its link with the hydrolytic product of S-methyl cysteine sulfoxide was only shown about 35 years later. S-methyl cysteine sulfoxide and its metabolite methyl methane thiosulfinate were shown to inhibit chemically-induced genotoxicity in mice. Thus, the cancer chemopreventive effects of Brassica vegetables that have been shown in human and animal studies may be due to the presence of both types of sulfur-containing phytochemicals (i.e. certain glucosinolates and S-methyl cysteine sulfoxide).

Eur J Endocrinol 1994 Aug;131(2):138-44

Antithyroid effects in vivo and in vitro of babassu and mandioca: a staple food in goiter areas of Brazil.

Gaitan E, Cooksey RC, Legan J, Lindsay RH, Ingbar SH, Medeiros-Neto G

University of Mississippi School of Medicine, Jackson.

Babassu (*Orbignya phalerata*), a palm-tree coconut fruit, mixed with mandioca (*Manihot utilissima*) is the staple food of people living in the endemic goiter area of Maranhao in Brazil, where goiter prevalence among schoolchildren was still 38% in 1986 despite an adequate iodine intake in most of the population. Therefore, the question arose as to whether or not the ingestion of babassu alone or mixed with mandioca contributed to the persistence of endemic goiter in this area of Brazil. In this investigation we examined the potential antithyroid effects of babassu and mandioca by means of in vivo studies in Sprague-Dawley rats, in vitro studies in porcine thyroid slices and using a purified porcine thyroid peroxidase (TPO) system. Samples of various edible parts of babassu and mandioca flour were homogenized and extracted in goitrogen-free water (GFW) for in vivo experiments, and in methanol (100 g/l), GFW or 0.06 mol/l phosphate buffer (pH 7.0) for in vitro experiments. The edible parts of babassu produced significant in vivo antithyroid effects ($p < 0.05$ - < 0.001) in rats on a high iodine intake (14 micrograms I- day⁻¹.rat⁻¹), as well as distinct and reproducible antithyroid and anti-TPO activities in both in vitro systems, their action being similar to that of the thionamide-like antithyroid drugs propylthiouracil and methimazole.

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MEDICAL TREATMENTS FOR GRAVES' AND HYPERTHYROIDISM

Following is an article written by Elaine Moore about the conventional medical treatments used for Graves' Disease and hyperthyroidism.

Conventional Treatment Options in Graves' Disease

By Elaine Moore, MT (ASCP)

Conventional and alternative medicine have identical goals when it comes to treating Graves' disease (GD). They both attempt to reduce the amount of thyroid hormone available in the blood. Because of their subtle action, alternative options are best reserved for patients with mild symptoms. Conventional options for GD, although more aggressive, are usually necessary for managing patients with moderate to severe symptoms.

Conventional medicine rapidly reduces certain overt symptoms which, if left untreated, could lead to severe complications, including thyroid storm. However, conventional treatment doesn't address the underlying causes. Also, both surgery and radioiodine ablation (RAI) cause hypothyroidism in more than 50% of treated patients. Spontaneous remission in GD (without treatment) occurs at a rate of 10% to 25% each year. And most GD patients eventually become hypothyroid spontaneously. These factors should be considered before deciding on treatment.

Conventional medicine offers three major options for treating GD: 1) the medical administration of antithyroid drugs (ATD's) which inhibit thyroid hormone synthesis, 2) partial or complete surgical removal of the thyroid gland, and 3) radioiodine ablation. The latter two options limit the amount of functional thyroid tissue capable of producing thyroid hormone. In this article I describe these treatment options along with another viable option, the use of ionic inhibitors. In addition, I describe beta adrenergic antagonists, a class of drugs often prescribed to manage symptoms of hyperthyroidism.

In the current (1998) edition of Williams' Textbook of Clinical Endocrinology, Larsen, et al recommend that several considerations be taken into account when deciding on treatment, including age, sex, general health, thyroid status, personal philosophy, and the preference of the physician based on his or her experience. Larsen, et al recommend that all patients use ATDs for at least 18 months before deciding on a permanent course of action.

Antithyroid Drugs

Antithyroid drugs (ATDs) have been a mainstay in the management of Graves' disease since their introduction in the mid-1940's. ATDs are reported to be extremely (at least 90%) effective in controlling the symptoms of Graves' disease. ATDs effectively inhibit thyroid hormone production. However, their effects aren't immediate. The stores of thyroid hormone present in the thyroid must be used up before symptoms subside. After several weeks, when these hormone stores are depleted, effects become noticeable.

ATDs also have an immunosuppressive effect giving this option a conventional advantage since immunosuppression influences the disease course, slowing disease progression. The drug PTU also inhibits the peripheral conversion of T4 to T3.

In the United States two antithyroid drugs are available for treating Graves' disease: Propylthiouracil (PTU) and Methimazole (1-methyl-2-mercaptoimidazole or MMI, Tapazole). In Europe, the Methimazole derivative Carbimazole is used. Since Carbimazole is rapidly metabolized to MMI, these drugs are essentially the same.

The choice of drugs depends on several factors. In pregnancy and in nursing mothers, PTU is preferred since it is less likely to cross the placental barrier and affect the fetus. If there are signs of fetal thyrotoxicosis, however, Methimazole is used since it can simultaneously treat fetal symptoms. PTU has been in use longer and is prescribed more often. Having a shorter half life (time when the initial concentration is reduced by 50%) of 75 minutes, it must be taken more frequently. The duration of action of PTU, however, is about 12 to 24 hours. At the onset of therapy, patients usually take PTU every 6 to 8 hours. The usual starting dose is 100 mg given 3 times daily.

Methimazole with its longer half life of 4-6 hours can be taken once daily. The starting dose is 20 to 30 mg. Patients on either ATD usually have a dosage change after 4-12 weeks. Methimazole causes euthyroidism quicker, taking four weeks, while PTU may take as long as 12 weeks. If there is no improvement, the dose is increased. With evidence that the drug is working (weight gain, reduction in goiter), the dosage is usually reduced.

Patients on Methimazole go into remission sooner than patients on PTU and are thought to have less trouble with side effects or eye complications. Although PTU is reported to be more expensive than Methimazole, several online patients have reported Methimazole as being significantly more expensive.

ATDs are used until patients go into spontaneous remission. Remission occurs as a result of the natural disease course although it may be amiably affected by the immunosuppressive effects of ATDs. Older patients (reported to usually have milder disease) and patients with small goiters usually go into remission sooner. Although there are reports of patients achieving remission after several weeks, 50% of patients achieve remission within 4 years. Relapses are more likely in the postpartum period.

If large ATD doses continue to be required for control, remission is considered unlikely. Autoantibody levels may be required to confirm this since sustained high antibody titers are also seen in patients unlikely to achieve remission. In this case, an integrative approach employing craniosacral therapy, traditional Chinese

medicine, acupuncture or other energy healing methods may prove to be beneficial. Also, the adjunctive use of ionic inhibitors has shown benefits in patients who show resistance to ATDs.

Although patients in Europe are kept on ATDs as long as necessary until remission is achieved, many American doctors are hesitant to do so and recommend a more aggressive approach if remission isn't achieved within 18 months. Cost containment is often a factor since patients on ATDs should be monitored closely every 2 to 4 weeks.

Side effects of both Methimazole and PTU are rare and include minor effects (seen in 1% to 5% of patients) such as rash, urticaria, arthralgia, fever and transient leukopenia (decreased white blood cell count). Rashes and hives should be reported to the doctor immediately. In most instances, treatment in the form of antihistamines is prescribed and the medication is continued.

There may also be rare gastrointestinal effects and rare (0.2% to 0.5%) major effects such as agranulocytosis where white cell levels become critically low. For this reason patients are advised to notify their doctor at the first sign of a sore throat or infection. At this time, a white blood cell count (WBC) is generally ordered. If the WBC count is critically low, the ATD is discontinued and appropriate antibiotics are prescribed. Other very rare side effects include aplastic anemia, thrombocytopenia (low platelet levels), and hypoglycemia. Hepatitis is a very rare effect and is seen only with PTU. Patients may be allergic to one of the ATDs, but patients are rarely allergic to both. PTU has also been recently listed in the same category as estrogen as a potential carcinogen. As with any treatment, however, the potential benefits must be weighed against potential risks.

Block and Replace Protocol

In the block and replace protocol, patients are kept on the usual starting doses of ATDs until they become euthyroid. Then, rather than decreasing the ATD dose, a low dose of thyroxine is added to the regimen. Patients following this protocol are thought to have more stable thyroid levels and they are less likely to become drug resistant. In the original studies of Yamamoto, thyroid function was assessed after one year by an RAI uptake scan. At uptake levels less than 25%, the drugs were weaned. This approach effectively predicted probable remission. With this protocol, remissions were reported to be achieved in more than 90% of patients.

Recent studies indicate that using ultrasonography as a tool to measure thyroid volume has the same predictive effect. Measuring stimulating TSH receptor antibody titers and comparing them to baseline levels also works. Without routinely used guiding factors, the block and replace protocol as used in the U.S. has met with limited success.

Surgical Thyroid Removal (Thyroidectomy)

Subtotal thyroidectomy is the oldest form of therapy used for GD. Surgery, both partial and total thyroidectomy, has the advantage of allowing direct tissue examination, and it offers prompt resolution of symptoms. After surgery, thyroid function returns to normal in between 90% and 98% of patients.

Thyroidectomy is a particularly good choice for patients with very large goiters since they seldom respond adequately to RAI. Surgery is also recommended for patients who plan to eventually become pregnant or patients who react severely to ATDs.

The surgical procedure most frequently used is a subtotal thyroidectomy in which a rim of each lobe is left, leaving a total of 4-6 grams. The thyroid is usually prepared to facilitate cutting by administering strong iodine solution for 7 to 10 days prior to surgery.

The mortality of thyroidectomy is close to zero. However, there are two rare complications, recurrent laryngeal nerve damage and hypoparathyroidism, which occur in 1% to 2% of cases. Both conditions can cause lifelong disability. Other transient complications include hypocalcemia, post-operative bleeding, wound infection, keloid formation, and scars. Finding a well experienced surgeon is of paramount importance.

Hypothyroidism is said to occur in 12% to 50% of patients in the first year after surgery, and late onset hypothyroidism develops in an additional 1% to 3% of patients each year, although this may be due to the natural progression of the disease. Recurrences may develop many years after surgery. 43% of recurrences occur within 5 years after surgery.

Radioiodine Ablation (RAI)

John Pacer, PhD, a physical chemist in Allentown, Pennsylvania, recently reminded me that radioisotopes are abundant in nature and work to maintain homeostasis by a process of natural selection. Radioisotopes are present in many fruits, including bananas and tomatoes, and in many types of wood.

Radioiodine, an isotope of iodine and a product of nuclear fission introduced in the mid-1940's, has become the most widely used treatment of adults with thyrotoxicosis in the United States. It is also the cheapest and fastest form of therapy and has the most potential to cause hypothyroidism. Radioiodine also releases autoantibodies into the circulation and heightens the immune response, exacerbating symptoms and contributing to a transient period of exaggerated symptoms. The release of stored hormone also causes a temporary exacerbation of symptoms. These effects may cause thyroid storm. One Graves' patient, Sharon, developed thyroid storm 5 weeks after her radioiodine ablation.

The isotope I-131 is usually used for ablation. It is administered as an oral dose either as a liquid where it is suspended in water or as a capsule. Thyroid cells can't distinguish between natural iodine and its radioisotopes so the thyroid follicular cells take up radioiodine in the same way they absorb iodine.

Inside the body, radioiodine atoms release energy in the form of beta particles and gamma rays, destroying or mutating whatever cells are at the end of their path length. The immediate effect of radioiodine is cellular

necrosis (death), which provokes an inflammatory response. Tissue studies show bizarre nuclear changes "reminiscent of carcinoma" which persist for many years.

Mutated cells are thought to be incapable of dividing although the increased rate of thyroid cancer mortality in ablated patients in the Cooperative Thyrotoxicosis Therapy Follow-up Study suggests otherwise. Since the cells of children divide at a greater rate than those of adults, mutagenic effects are more pronounced in children. Although there are no long-term studies on children treated with radioiodine, an increased incidence in adenomas in children treated with external radiation has been demonstrated in more than one study. Thus, radioiodine is contraindicated in children and women of childbearing age.

Although radioiodine is said to have a half-life of 8 days, it is thought to take 8 to 10 cycles before all of it leaves the body. Dr. Pacer emphasized that side effects as well as the time radioiodine actually leaves the body are dose related. If trillions of atoms are initially delivered, imagine how long the reduction would take. Dr. Joseph Gong, a cell biologist who studies the cumulative effects of radiation, says that radioiodine never fully leaves the body. And the contributions from particles which do exit the body provide a total body dose. A recent review of data from England's Whickham Study shows a small but significant increase in both thyroid and small bowel cancer mortality in ablated patients.

There is no optimal dose for RAI. And protocols for determining an optimal dose are controversial. Whatever method is used, calculations should take the thyroid volume and radioiodine uptake test results into consideration. One recent European study recommended that doses not exceed 7,000 rad (70 Gy) if early hypothyroidism is to be avoided. Higher doses are associated with severe hypothyroidism. Thyroid function is reported to gradually decline within weeks to months after radioiodine treatment.

Radioiodine ablation has also been found to induce and/or exacerbate Graves' ophthalmopathy (GO) and pretibial myxedema. A short course of prednisone used in conjunction with radioiodine helps in preventing the development of GO.

Although radioiodine is effective, its use is not without risk. And in many instances, it 's a form of overkill. I'm currently working on a project aimed at determining long-term chromosomal damage caused by RAI which is demonstrated by an increased number of red cells with transferrin receptors. I'll share results on this board sometime in the next 6 months.

Ionic Inhibitors

In addition to the 3 major options, conventional medicine for GD occasionally employs ionic inhibitors, chemicals such as potassium perchlorate, which work like anti-thyroid drugs. At one time, these agents were used in extremely high doses which caused aplastic anemia and gastric ulcers. Since, they've been found to be effective at much lower doses. In the last decade, potassium perchlorate has been used with success in daily doses of 40 to 120 mg. Potassium perchlorate is also used in conjunction with ATD's to treat iodine induced thyrotoxicosis and it's effectively used in patients who are resistant to ATD therapy when ATDs are used as the sole agent.

Beta Adrenergic Blocking Agents

Beta adrenergic antagonist drugs are an integral part of the treatment protocol in Graves' disease. Although they have no direct effect on thyroid function, they are valuable in ameliorating cardiac and nervous symptoms. While propranolol was the first drug of this class used to treat thyrotoxicosis, newer cardio selective agents such as esmolol, atenolol and metoprolol are also prescribed. Propranolol is primarily used since it has the advantage of inhibiting the conversion of thyroxine (T₄) to the more potent triiodothyronine (T₃).

Although propranolol is contraindicated in patients with bronchospasm and asthma, cardio selective drugs may be used in mild cases. Beta blockers are also contraindicated in congestive heart failure except when the heart failure is rate related or caused by atrial fibrillation. In diabetes, beta blockers are contraindicated because they may mask hypoglycemic symptoms. Beta blockers should not be used in patients with Brady arrhythmias, Raynaud's phenomenon or to patients undergoing treatment with monoamine oxidase inhibitors.

While effective in improving negative nitrogen balance and decreasing oxygen consumption, heart rate and cardiac output, beta adrenergic blocking agents are seldom able to restore these measurements to normal except in the mildest cases. For this reason, they are seldom used as a primary agent. Their value is in the management of symptoms while treatment is being decided on and as a complementary agent.

Beta adrenergic antagonists are tolerated well although at high doses they may cause drowsiness. Common side effects include nausea, headache, fatigue, insomnia and depression. Beta adrenergic agents, especially when used at high doses, must be not withdrawn abruptly. Abrupt withdrawal may be followed by an exacerbation of symptoms of hyperthyroidism, including thyroid storm.

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HAIR ANALYSIS

- **WHERE TO GET AN ANALYSIS.** (If you have a good source and don't see it listed here send all the information to BU007@aol.com and I'll get it listed.)
- **HOW TO INTERPRET THE ANALYSIS.**
- **HOW TO STRUCTURE A SUPPLEMENT PROGRAM TO CORRECT THE DEFICIENCIES.**

Hair analysis is probably the best way to determine if you are deficient in minerals. Blood analysis is appropriate for determining certain minerals like iron, but generally blood analysis is much more expensive than hair analysis. Hair analysis has been maligned in the press over the last few years but it has been studied extensively and the interpretation of results is getting much better. Interpretation is important because high levels of a mineral in the hair doesn't always mean that the mineral is high in the body. In this section we will talk about where to go to get a hair analysis, interpreting hair analyses, and how to structure a supplement schedule based on the hair analysis results.

WHERE TO GET A HAIR ANALYSIS.

1. Dr. Larry Wilson (email him at: Larry@drlwilson.com). Dr. Wilson uses Analytical Research Labs in Phoenix, Arizona. He has performed and interpreted many thousands of hair analyses and has written a textbook for teaching health professionals how to interpret hair analysis results. His book is called *Nutritional Balancing and Hair Mineral Analysis*, is available from many stores. One can special order it through Amazon.com or other book stores. Two places that stock the book are: Natural Books and Products in Escondido, CA 1-888-743-1790 and Endomet Labs at 1-800-528-4067. It's a good book to own. Dr. Wilson and I have disagreements about many things in relation to copper metabolism and thyroid disease, but he has extensive knowledge and is a very valuable source of information. If you tell him you're a member of the hyperthyroidism group he will charge you \$100 for the analysis. This is reasonably inexpensive way to get an analysis because you don't have to go to a local doctor and pay for an office visit. Just email him for instructions. When you get the results you can fax me them to me at 818-889-6969 or email me for a mailing address (BU007@aol.com). I would suggest using the supplement suggestions on this site rather than those from Dr. Wilson. Dr. Wilson wrote to me saying, "Your readers might want to know that hair analysis tests from Great Smokies Lab, King James Laboratory, and Doctors Data will give significantly different results because they wash the hair in acetone and detergent. Analytical Research Labs and Trace Elements, Inc do not wash the hair. In the JAMA study referred to by Dr. Mercola, the labs that wash the hair produced erratic results. This is also what was found in earlier studies. Hair is biopsy material and harsh washing chemicals damage it. That is a main reason I use ARL (Analytical Research Labs)."
2. Analytical Research Labs, Inc. Phone: (800) 528-4067 or (602) 995-1580. I don't know if you can get an analysis directly from them without going through a doctor, but I will find out. Anyone know?
3. Great Smokies Diagnostic Laboratory. Go to their website at www.gsdl.com and write to them and ask for a list of health professionals in your area who use their lab. Their analysis is more extensive than many labs. I have talked to one of their research scientists about analyzing for additional minerals that I feel are important in thyroid disease and they seem open to that possibility.
4. King James Medical Laboratory. Go to their website at: <http://www.kingjamesomegatech-lab.com/> Phone number is (800)437-1404. Just ask for a kit to be sent and it is self explanatory on what needs to be done. The cost is \$39.
5. From Pat: You can order a hair analysis kit for \$70 from Johnson Drugs in Waltham, MA. <http://www.Johnsondrugs.com>

The hair analysis company is Doctors Data.
<http://www.doctorsdata.com>

When the hair analysis comes back to the pharmacy, the pharmacist Gary Krakoff will call you and interpret it to you over the phone for no further charge. Then he will mail it to you. Gary tends to emphasize toxic elements load in his interpretation.

6. Hi, I haven't posted for a while but agree John's ways work! I have come to believe that the hair tissue mineral analysis is one of the most helpful tools to know what is going on in our bodies. I am now working with Anamol Laboratories here in Ontario Canada. They have been honoured as one of the most respected nutritionally -oriented testing laboratories in North America. Their list of satisfied customers include practitioners from Europe and Latin America , as well as across Canada and the United States. If anyone is interested in a hair analysis ,I am able to send you the kit with complete instructions . You return to me with hair sample and I then forward to Anamol Laboratory. They test for 38 elements and provide a thorough explanation. I am able to provide this for \$ 59.00 Canadian which would be a fair bit cheaper for you US folks at approximately \$38.00 US. If interested please contact me privately at huyben@quadro.net and I will send you a kit.

I have great news ! I have spoken to Dr Tamari of Anamol Laboratories and they have agreed not to wash hair samples that I send in .
Now I can provide the folks on this site with a reasonably priced hair analysis that isn't washed before testing that test more elements than most labs.

HAIR ANALYSIS INFO FROM HYPERS:

The following is information on Swan's hair analysis. I agree with Swan's analysis that she is deficient in selenium. Because both her zinc and iron appear to be high in the ratios, this suggests to me that she is deficient in copper. Also, the laboratory recommendations on the calcium/magnesium ratio (7:1) are different from the recommended ratio to take. Most supplements are 2:1 (cal:mag) but 1:1 seems to work better for most hypers. This is for correction purposes and not intended to alter the body's ratio to 1:1.

FROM SWAN:

Hi, I wrote about the hair analysis report in March. I want to expand on it. It's neat that it has a page of ratios like: The lab has its own ratios to compare to now and optimum. It is, of course can not be expected to be, not like John's supplement list.

This can give a person an idea though of the ratios we are talking about on the page. I have only started supplements around January 2000.

Calcium:Magnesium mine 8:1 Labs suggests 7:1 John suggests 1:1 particularly if having heart palpitations
Zinc:Copper (mine 18:1) lab suggests 7:1, I take 4:1 daily, Zinc:Selenium (mine 609:1) lab suggests 88:1
Zinc:Manganese (mine 448:1) lab 250:1 Zinc:Lead (mine 772:1) lab 250:1 Selenium:Mercury (mine .3:1) lab suggests 100:1 Selenium is DEFICIENT! Iron:Aluminum (mine 2:1) lab suggests .6:1 Iron is over the limit here Calcium:Phosphorus (mine 4:1) lab suggests 4:1 Calcium:Lead (mine 1365:1) lab suggests 679:1

I can tell that selenium as well as chromium are deficient in a big way. It may be years before I build it up for storage too. I am in the normal range for TSH now so those using the supplements to really help attain remission could benefit by knowing their own levels.

I would be interested in seeing other's ratios. Swan

Sci Total Environ 1994 Dec 1;156(3):235-42

Heavy metals in human hair samples from Austria and Italy: influence of sex and smoking habits.

Wolfspurger M, Hauser G, Gossler W, Schlagenhaufen C

Institute of Nutrition, University of Veterinary Medicine, Vienna, Austria.

Hair samples from 79 young healthy adults from Vienna (Austria) and Rome (Italy) were analyzed for As, Cd, Co, Cr, Ni and Pb by ICP-MS. No differences were found between the two locations except for chromium, which was significantly higher in the Viennese population ($P < 0.001$). In both cities male hair contained higher arsenic ($P < 0.001$) and lower cadmium ($P < 0.05$) levels than female hair, and in Vienna lead concentrations were lower in males ($P < 0.05$). Striking differences appeared when smokers were compared with non-smokers. Geometric means (micrograms/g) of smokers versus non-smokers were: arsenic 0.081 vs. 0.065, cadmium 0.075 vs. 0.038 ($P < 0.05$), cobalt 0.025 vs. 0.010 ($P < 0.05$), chromium 0.84 vs. 0.72 ($P < 0.05$), lead 3.42 vs. 1.47 ($P < 0.001$) and nickel 0.64 vs. 0.32 ($P < 0.005$). Consideration of a large number of biological and behavioural factors minimizes bias inherent in unmatched sample composition.

The following is from Dr. Mercola's website, www.mercola.com:

Hair Mineral Analysis

JAMA published a [negative study](#) on hair analysis this past January regarding the clinical use of hair analysis. It was an incredibly poorly designed study and I was surprised to see that it was even published.

For the first fourteen years of my practice I was opposed to hair analysis testing as I bought the "traditional" perspective on this tool.

Later, I learned from some skilled clinicians, that this was indeed a useful clinical tool. However, it appears the issue complicating optimal interpretation, and what has seriously confused the issue of hair analysis, is the practice of washing the sample prior to analysis.

There are only two labs that I recommend using for proper readings for hair analysis. Trace Elements and

Analytical Research. Both labs are based on the work of Paul Eck.

The major distinction from other hair analysis labs is that they don't wash their samples prior to the analysis. As far as I can tell all the other labs wash the hair and this has a tendency to disturb some of the essential mineral ratios. It does not seem to make much of a difference for the toxic metals.

If you are a licensed health care professional I have made special arrangements with Analytical Research to provide you with three free kits to see how you enjoy their service. The only thing you need to do to obtain your kits is to call them (602-995-1580) and mention that you were calling regarding the special offer you saw on my web site.

They provide educational materials but they also have a book "Nutritional Balancing and Hair Mineral Analysis" for \$18 written by Larry Wilson, MD, that helps one understand the biochemistry behind hair analysis.

The analysis has specific nutrient recommendations, mostly minerals. One can obtain them from the company, but I find that it is much easier to use the ones we, or the patient already has. I am amazed at how many people do not actually need to take calcium based on this analysis. It is quite a remarkable way to identify which minerals a person needs to build their bones.

This offer is ONLY available to licensed health care professionals.

JAMA Letter to the Editor; March 28, 2001 285(12):1576-7

Dr Seidel and colleagues (1) found that there is **excessive variability between laboratories in the results of hair analysis**.

This study should not be represented as a final, rigorous, and decisive condemnation of the entire commercial hair analysis industry, as **other studies have established the validity of hair analysis evaluation**. (2-6)

The study by Seidel et al simply shows that there is some variation among the laboratories' results, as would be expected. The study's design was **critically flawed** in several areas.

The authors compared test results and reference ranges for laboratories using different methods. They also failed to distinguish between accurate and inaccurate laboratories, as they did not use a specific standard or reference laboratory.

The authors' inclusion of a noncertified, unregulated, and illegally operating laboratory that represents **less than 3%** of the total hair analysis activity in the United States introduced **bias and error** into the analysis and conclusions. This unregulated laboratory was responsible for 12 of the 14 "statistically significant ($P < .05$) extreme values" cited in the study.

Furthermore, the bias of this study is further evident as the authors did not adhere to their own stated laboratory selection protocol.

This resulted in a certified laboratory with a significantly higher monthly sample volume not being included in the study in favor of the small uncertified laboratory that reported extreme and dubious measurements.

It should also be noted that blind proficiency testing, such as was used in this study, is the most stringent form of laboratory evaluation, so stringent in fact that it is rarely used in clinical laboratories.

Modern clinical proficiency testing is overt in that the test specimens are identified as such. This fact coupled with the absence of any criterion standard for identifying correct incorrect test results seems designed to **unfairly target the entire hair analysis industry**.

Such a standard applied to most clinical tests would result in similar findings.

We do acknowledge that this limited study does raise some challenging issues that the industry must deal with, such as, the identification of laboratories misrepresenting themselves as certified and yet operating illegally. Most commercial hair analysis companies, however, are on record for proficiency testing initiatives, data comparison, and clinical case presentations involving hair elemental analysis.

Joseph M. Mercola, DO
eHealthy News You Can Use
Schaumburg, IL

David L. Watts, PhD
Trace Elements Inc
Addison, TX

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HEMOCHROMATOSIS

Hemochromatosis is the excessive buildup of iron in the body, especially noted in the liver. It appears to me that hemochromatosis is the result of a copper deficiency.

While there appears to be a hereditary form of the disease, there may also be a dietary form. While many people think that there is some genetic damage which causes the hereditary form, I think that it is most likely a genetic adaptation which enables the offspring of persons eating a high copper diet to increase copper excretion to maintain normal levels. When these offspring then have a diet low in copper, they develop a copper deficiency and this can lead to hemochromatosis for those eating a high iron diet (high red meat or fruit diet).

It is my belief that persons with high iron from hemochromatosis should supplement with copper and reduce their high iron intake to get these two minerals balanced. Increased zinc might also be appropriate in individuals with adequate copper, since zinc will reduce iron levels also.

The following study indicates that excessive vitamin C intake may be a contributing factor in hemochromatosis. Vitamin C increases iron absorption while at the same time it seems to have an effect in decreasing copper. This copper decreasing effect could be the direct result of increasing iron absorption or it could be an independent effect.

Int J Vitam Nutr Res 1999 Mar;69(2):67-82

High-dose vitamin C: a risk for persons with high iron stores?

Gerster H.

Vitamin Research Department, F. Hoffmann-La Roche Ltd, Basel, Switzerland.

The contribution of vitamin C (ascorbic acid) to the prevention of iron deficiency anemia by promoting the absorption of dietary non-heme iron-especially in persons with low iron stores--is well established. But the question has been raised whether high-dose intakes of vitamin C might unduly enhance the absorption of dietary iron in persons with high iron stores or in patients with iron overload, possibly increasing the potential risk of iron toxicity. Extensive studies have shown that overall the uptake and storage of iron in humans is efficiently controlled by a network of regulatory mechanisms. Even high vitamin C intakes do not cause iron imbalance in healthy persons and probably in persons who are heterozygous for hemochromatosis. The uptake, renal tubular reabsorption and storage of vitamin C itself are also strictly limited after high-dose intake so that no excessive plasma and tissue concentrations of vitamin C are produced. The effect of high-dose vitamin C on iron absorption in patients with iron overload due to homozygous hemochromatosis has not been studied. Of special importance is the early identification of hemochromatosis patients, which is assisted by the newly developed PCR test for hereditary hemochromatosis. Specific treatment consists of regular phlebotomy and possibly iron-chelating therapy. These patients should moreover avoid any possibility of facilitated absorption of iron and need to limit their intake of iron. Patients with beta-thalassemia major and sickle cell anemia who suffer from iron overload due to regular blood transfusions or excessive destruction of red blood cells need specialized medical treatment with iron chelators and should also control their intake of iron. The serum of patients with pathological iron overload can contain non-transferrin-bound iron inducing lipid peroxidation with subsequent consumption of antioxidants such as vitamin E and vitamin C. The role of iron in coronary heart disease and cancer is controversial. Early suggestions that moderately elevated iron stores are associated with an increased risk of CHD have not been confirmed by later studies. In vitro, ascorbic acid can act as a prooxidant in the presence of transition metals such as iron or copper, but in the living organism its major functions are as an antioxidant. High intakes of vitamin C have thus not been found to increase oxidative damage in humans. Accordingly, the risk of CHD or cancer is not elevated. On the contrary, most studies have shown that diets rich in vitamin C are inversely related to the incidence of these diseases.

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HERNIA

February 22, 2002

(I thought today would be a good day to write out this information, while I still feel the pain from my latest hernia surgery.)

My belief is that hernias are the result of nutritional deficiencies, as opposed to the common theory that they result from heavy lifting. Copper deficiency is most likely the key deficiency which causes hernias.

Copper is essential for collagen production and when copper gets deficient, then the collagen fibers get weak. Collagen provides the structure which holds the muscle fibers together, so this weakening can result in a separation of the muscle fibers, allowing the inner tissues to protrude.

There are many types of hernias and these can occur in persons of any age, including newborns. I have had two inguinal hernias: the right side in 1993 and the left side in 1997. Each was repaired using a polypropylene mesh (brand name Marlex) as a reinforcing material.

My surgeon told me that hernias repaired without a mesh have about a 16% chance of recurring, while those with the mesh repair recur only about 2% of the time. I was concerned about the possibility of having some reaction to the mesh, but he informed me that there was nothing to worry about.

The hernia repair I had done on the right side in 1993 went well and I never had another problem with it. I had waited about 7 years (not a typo!) from the time I first developed the hernia to the time when I had it repaired. Interestingly, I developed the hernia during one of my fasts. I was fasting because I wasn't feeling well. Most likely I had a copper deficiency and should have been supplementing with copper rather than fasting! I tried many suggested therapies to correct the hernia naturally, but none of them worked. I managed to get along by not eating before any physical activity. If my colon contents were minimal, I was usually able to play basketball or hike without problems. However, if I had eaten I'd have to constantly push the hernia back in.

The hernia repair I had done in 1997 went smoothly also. I didn't wait very long to have this one repaired, since I had success with the previous repair. However, this repair came back to haunt me four years later. Also, of note: this hernia repair was performed just a few weeks before I started developing hyperthyroidism. I don't think there was a causal effect from the operation or the mesh, but who knows. Most likely I had a copper deficiency which was the major factor in both the hernia development and in the hyperthyroidism.

In late June, 2001, I started getting a soreness in the left groin area. Right where the diagonal scar from the '97 hernia surgery was, it started to swell, get sore, and turn red. Within two weeks the sore opened and started draining. This is when I started doing research about mesh rejection.

Apparently there is a problem with mesh rejection since it's in the medical literature. Various studies have shown that between 1 and 4 people per thousand will reject the mesh. The standard medical treatment for mesh rejection is surgical removal of the mesh.

At first I thought, "What luck...I was that one in a thousand....", but the more I thought about the rejection problem, the more I realized that I'd be the person to get it. I have never been the type who has allergies or other problems like that, so I didn't think that it was because my body was too weak to tolerate the foreign object in my body. My thinking was that it was the opposite: my body was very strong and well nourished and had the energy to push out any foreign object.

What I have done with my nutrition since developing this hernia is quite different from what most people do. Supplementing with copper and other nutrients that support thyroid and collagen health has significantly changed my body chemistry. Most people don't do this.

By supplementing with copper, my body now has the capacity to rebuild the tissue where the hernia occurred. This means that as it rebuilds the tissue, it gradually pushes the mesh out.

With this theory in mind, I decided to wait as long as I could before getting the mesh taken out. I was actually hoping that my body would push the mesh fully out of my body so I could avoid surgery. I would have to change the bandage twice a day and the gauze would be covered with greenish fluid. I thought that this fluid was the mass of dead cells that died on one side of the mesh, while new cells were being generated on the other side, a process which gradually moves the mesh toward the skin surface.

However, after eight months the sore hadn't made any progress. Also, I had a trip to the tropics coming up in a couple weeks and I didn't like the idea of going to a place where germs proliferate like crazy when I had an open wound.

I had a problem finding a surgeon. The problem is that most of them have never dealt with this type of problem and the few that have done so have only seen one case. I finally found someone who seemed competent, but he hadn't done a mesh removal since he was a resident, 30 years ago.

This doctor told me that he thought that it was unlikely that my body would be able to eject the mesh. The mesh used is roughly an oval with a slit cut to the center from one edge. This slit enables the patch to be placed around the seminal

About a week ago, the area became increasingly sore and it seemed that a change was occurring. I thought that the mesh had been migrated sufficiently so that it was pulling on the seminal vesicle and this tension was causing the increase in pain. This worried me.

Yesterday I had the mesh removed in an outpatient surgery center. Everything went great and now, barely 24 hours after the surgery I'm feeling quite well.

The surgeon told me that he was very surprised because everything inside looked much better than he had expected. The mesh was not attached at the center and barely attached around the edges. It was quite easy to get it out. He told me that the original hernia hole was nearly all filled in with new tissue and that it just took a couple sutures to close the small hole that remained. While before the operation, he warned me that there was probably about a 20% chance of needing a subsequent hernia repair, after the operation he told me that this was extremely unlikely and that everything should be fine.

Of further interest he told me that the mesh was not attached to the seminal vesicle and that it eventually would have been pushed out of my body. So what I originally hoped for so many months ago, would have happened if I'd had just a little more patience.

However, right now, I'm glad I got it taken out. It was another great medical experiment on myself, and I really believe that my waiting all that time gave my body the time to close the original hernia.

Of course, I'm very happy that I discovered copper and its critical function in collagen formation. Without that, I might not have had a mesh rejection, but then I wouldn't be as healthy as I am now. Hopefully going through this ordeal will yield information that will help others with similar problems.

Here is what I'd recommend:

1. Make sure you have adequate copper to make sure you don't get a hernia. Routine hair analyses are the only way to determine your copper status. Blood analysis won't show it.
2. If you get a hernia, take copper and the assisting nutrients (follow the supplement information for hypsers). You might want to wait to see if the hernia will repair itself, if this is not a danger to your health. I now believe that it's possible the body can repair this problem if you give it the nutrients it needs.
3. If you elect to get the hernia repaired surgically, you'll need to decide if you want the mesh or not. Some doctors don't use the mesh so you'll want to find one of these. If you get the mesh put in, be aware of a possible mesh rejection if you are supplementing copper and other nutrients that assist collagen formation. If mesh rejection does occur, I'd suggest following the path that I took. Wait as long as you can for your body to repair.
4. If you get a hernia, find a good surgeon and use his expertise to avoid getting yourself into trouble. They are usually able to tell you if you are at any risk of complications if you delay surgery. Get multiple opinions.
5. Remember if your parent had a hernia (like my father), or you are tall, you might be at greater risk of developing a hernia. Also, if you have had a hernia, your children are probably also at risk of a copper deficiency. Supplement with copper if you have determined that you might be deficient.

I hope all this information helps you. Please email me at BU007@aol.com or post on the bulletin board if you have any relevant stories. Then I can post them below. Thanks, John

Studies:

This one is interesting, but I don't understand the implications.

Hum Pathol 1985 Nov;16(11):1141-6

Crystalline foreign particulate material in hernia sacs.

Pratt PC, George MH, Mastin JP, Roggli VL.

The subserosal stroma of hernia sacs consistently contains birefringent particulate material, in amounts greater than those observed in other intra-abdominal organs. The major component of this material was shown in the present study to be talc; thus, it cannot be of endogenous origin. Cellular response to this foreign material is remarkably slight. Possible sources of the material and mechanisms of access to the hernia sac were examined in a search of the available literature. It is proposed that the probable source is ingestion with food or, more likely, medications and that the particles reach the peritoneal cavity by migration through the intact intestinal wall. They probably reach the hernia by sedimentation in peritoneal fluid and subsequently migrate into the subserosa. The virtual absence of response to the particles is attributed to their composition (silicate) and their relatively small size (up to about 10 microns) compared with the particles in talc granulomas (up to at least 50 microns).

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RECOVERY FROM HYPERTHYROIDISM

My hyperthyroidism began in July of 1997. I was 53 years old and feeling really great, exercising a lot, bodybuilding, and taking numerous supplements such as ginseng, pine bark (Phytonol) and grape seed extracts, free amino acids, L-carnitine, DHEA (100 mg/day), pregnenolone, Co-Q-10, ginkgo biloba, L-arginine and L-ornithine, kotu kola, various testosterone boosting herbs, primrose and fish oils, garlic capsules, melatonin at night, nearly complete vitamin and mineral supplements, 8-10 grams of vitamin C, and had just started taking creatine for muscle building. I was flying high and felt tremendous. I played full-court basketball three times a week, roller bladed, hiked, mountain biked, lifted weights, generally exercised about 4 hours a day, and had a high sex drive.

I had just bought a new aluminum road racing bike, was riding 50 miles 2-3 times a week, and was enjoying racing other bikers at the beach. One day as I was going all out on the bike I felt a weird flutter in my heart so I let up and it went away. It kept recurring and within a few weeks I was waking up in the early morning with a few minutes of rapid heart beat. Over the next couple of months it got worse and I gradually quit taking the long list of supplements I was using in an effort to determine if one of them was the cause.

By the beginning of October I was having difficulty exercising because my heart would start racing too fast and I'd have to stop and rest. I started keeping a diary of all my food and supplement intake, activities, and a record of how I felt. I found that some foods like pasta and salads with ample fresh-pressed garlic seemed to aggravate my condition. Some foods seemed to bother me and some helped, but I couldn't make sense of the whole situation. As I gradually eliminated more foods and more nutritional supplements, I got sicker and sicker.

By the middle of October I was really sick, having periods of rapid heart beat, violent shaking, and sweating at all times of the day. I'm talking about total "will I live or will I die" panic!! I would walk around, breathing deep, until they passed. These were episodes that I would later learn were "thyroid storms." I didn't know it at the time, but these storms can be extremely serious. It's not unusual for the heart rate to get up to 150 beats per minute or more. Some people have heart attacks and some people die.

At this point I couldn't exercise at all. When I tried to play basketball I would get red and my heart rate would escalate to the point where I had to stop after only a couple minutes. The slightest thing would send my heart racing. In just a few weeks I had lost about 20 lbs from my already lean body and lost 1/3 of my muscle strength.

I have a nutritionally oriented doctor and went to see him. Blood tests showed extremely high thyroid levels and TSH near zero. Ultrasound showed definite abnormalities in the structure of the thyroid. He put me on PTU, a drug to counter the overactive thyroid, and recommended a radioactive iodine test to see what was going on in my thyroid.

After 4 days on PTU I discovered that by taking very large quantities of calcium and magnesium, I could control the thyroid storms and rapid heart beat. Whenever my heart started racing, I would take 6 cal/mag capsules and within 20 minutes I'd get relief. I was able to stop taking the PTU and never did go in for the radioactive iodine test. I consider my doctor an excellent nutritionist but he told me there was no cure for hyperthyroidism, only management. In fact he told me the same thing that many nutrition books say, to increase my zinc consumption. When I tried this my hyper symptoms increased even more.

I was extremely concerned about my condition. I had always been my primary doctor and had studied nutrition for 27 years. I had managed to overcome every health problem that I had ever faced through nutrition, but this was a very unique and perplexing situation. Nearly every supplement that I tried caused my hyper symptoms to increase. Before long it seemed like I couldn't find anything that was helping, so I started reading everything and experimenting on myself to find the cause and cure.

One of my first attempts at solving the problem was to do what I always have done when I got sick in the past--use a combination of raw foods and fasting. Much to my surprise, eating only raw foods for 4-5 days and complete fasting for 3 days only made my condition worse. This helped convince me that I was dealing with nutritional deficiencies. The mystery was what was I deficient in?

Gradually I started finding things that helped. I started taking 6 capsules of calcium/magnesium (I found Solaray's Calcium/Magnesium Citrate best--6 capsules provide 1000 mg of cal and 1000 mg of magnesium--most cal/mag supplements have a 2:1 ratio, but the 1:1 ratio seemed much better) every 4 hours, 24 hours a day, and sometimes up to 36 capsules a day. I also eliminated all iodine from my diet. This controlled the storms of rapid heartbeat, but I didn't seem to be getting any better.

The magnesium is extremely important. About three months before I developed hyperT, I began having neck pain and stiffness. I didn't think much about it, but when I found that I had hyperT, I started getting chiropractic adjustments. They didn't seem to help, but by mistake I got a supplement from my chiropractor that he told me was calcium and magnesium. After three days taking it I felt much worse with more severe rapid heart rate. I had the chiropractor check with the manufacturer to see if there was magnesium in the supplement. He reported back to me that that batch contained only calcium. Through this mistake I found that calcium without magnesium makes the hyper symptoms much worse. The magnesium is more important

than the calcium.

One morning I was really desperate. I was feeling terrible and spent the morning poring through nutrition books looking for some clue. I read about biotin and although the book stated that there had never been a documented case of biotin deficiency in someone who wasn't eating raw egg whites, the symptoms of biotin deficiency sounded a lot like what I was experiencing. I read that egg whites contain avidin which is a substance which binds with the B vitamin biotin preventing the body from being able to use it.

That morning I also took (2) 2 mg Copper, selenium, and some liquid trace elements. I was desperate and scraping the bottom of the nutritional barrel. At lunch I barely had any appetite and ordered a small cup of bean soup. I took a couple biotin tablets. Before long I started feeling better and my appetite returned. I ordered more soup and wound up eating a good sized meal for a change. The next morning I entered the following in my diary, "Feeling Better!! Pretty sure I had a copper deficiency which caused my hyperthyroidism."

I started taking copper supplements every day (at this point I didn't realize the trace minerals were important), but I didn't feel any better and concluded that it wasn't a copper deficiency. I took copper on and off for the next few months. I was gradually improving but never made the association between taking copper and improving because I was experimenting with so many different things in a desperate effort to get better.

For awhile, I thought that maybe I had aluminum poisoning. My hair mineral analysis showed high levels of aluminum and I reasoned that I might have ingested aluminum from my bike when peeling and eating oranges without first washing my hands. There is a possibility that excess aluminum contributed to a depletion of copper.

I felt poisoned and kept looking for something in my food or environment which might be toxic. Now I feel that mineral deficiencies resemble poisoning because a deficiency of one mineral allows other minerals to be in excess. This has been my history: when I get sick I always think I'm poisoned so I go on a raw food or fruit diet or fast and stop my supplements. This has always made my condition worse until I've discovered my deficiency and rectified it.

Over the next few months I experimented with a large number of supplements, taking them for a while and then stopping. I was gradually feeling better but didn't know why. I would occasionally have a great day, being able to exercise without heart problems and then would have a long bad period. Gradually I gained weight and put back the 20 lbs. I had lost. By December I was feeling better overall, but still having bad days.

By April, 1998, I had read everything I could find on thyroid and experimented with just about every supplement available. I found that there is virtually no helpful information anywhere on hyperthyroidism. On April 23 I read Joel Wallach's book, "Rare Earths and Forbidden Cures." Wallach has spent his life researching diseases caused by mineral deficiencies and in a table of copper deficiency diseases, he listed hyperthyroidism and hypothyroidism. Hyperthyroidism was not listed in the index, so it took a mineral by mineral study to find this information.

Wallach says that a copper deficiency is very serious and can lead to life-ending liver disease and instant-death aneurysms besides causing hyperthyroidism and hypothyroidism. One of the first indications of deficiency is white hair. I started studying my diary for correlations between taking copper and feeling better. I did find a correlation, but it was with taking both copper and trace minerals at the same time. I immediately started taking copper and trace minerals and found that within hours I felt better!! I also found a correlation with feeling better after taking boron, so I started taking 6 mg of boron daily. Only recently have I found that boron supplementation increases estrogen and testosterone, thereby lessening the effect of excessive progesterone.

The reason it had taken so long to find what was helping me was that it was a combination of minerals. When I had taken the copper by itself I had felt better a day or two later, but when I took it with trace minerals I felt better right away. Apparently there are a group of minerals in the trace element supplement that work with copper to regulate the thyroid. It's possible that one of these beneficial minerals in the trace mineral supplement was boron, but it's also possible that there are more.

I tried to cut down on the amount of cal/mag that I take but found that I still needed about 18 capsules a day. If I take less, I start getting pains in my teeth. Silicon is also supposed to assist cal/mag utilization so I also took that. I have gradually been getting better and my last symptom of a few minutes of rapid heart beat when I first wake at about 4-6 am has gradually decreased. I had been taking (2) 2 mg of copper a day since April and in the middle of August I doubled it to 4 a day (8mg) as an experiment. At the beginning of September I increased the copper to 12 mg and have felt even better. (The Nutrition Almanac states that people can safely take up to 35 mg of copper a day.) I take 6 tablets of Mezotrace brand trace elements daily. I was also taking up to 100 mg of zinc a day, but have since experimented and feel that taking this zinc probably delayed my recovery from hyperT. Stopping zinc for two weeks recently eliminated all symptoms and I recently recorded my resting heart rate at 43 beats per minute--a long way from the usual 90-100 and up when I had hyperT. I started taking zinc again, but a lesser amount, and now take 5-8 mgs of copper a day.

An interesting thing happened in June. One morning I woke up early feeling terrible. My heart was beating

very slowly and I was cold and exhausted. I was really bad off for about a day until I realized I had gone hypothyroid because of my strict iodine restriction. I started taking kelp tablets and felt better in about 4 hours. Be aware that if you restrict your iodine intake as I did, the same thing can happen to you. That is why I now recommend reintroducing kelp or iodine as soon as the hyper symptoms subside. If you were to take kelp without copper, there is the possibility of aggravating your hyperthyroidism, but after you've been taking copper (and selenium) for awhile, you shouldn't have a problem with iodine. Some books, including my endocrinology textbook, state that hyperthyroid symptoms can be alleviated with massive doses of iodine and that doctors sometimes use that technique. That may be possible but I wouldn't recommend doing that.

Now I feel great and can exercise as much as I want--full-court basketball for three hours or a 50 mile bike ride--no heart problems at all. The only remnant of the disease at all is a slight feeling in my thyroid gland which is gradually disappearing.

I feel that the most important deficiency that I had was copper and when I look back at my diet I understand how I became deficient. The foods high in copper are shellfish (oysters, clams, crab and lobster), organ meats like liver, dried fruits like raisins and dates, beans, beer made in copper vats, and chocolate. I had avoided many of these foods because I thought they were bad for me. I was avoiding dried fruits and chocolate as much as possible.

Another result of copper deficiency is copper-deficiency anemia, which is similar to iron-deficiency anemia. This would explain why people with hyperthyroidism have such low levels of physical and mental energy. They call it "brain fog". I remember feeling the lethargy and inability to think when I was sick. My present mental clarity is such a contrast to my foggy thinking during hyperthyroidism, that I'm amazed that I was able to figure out what was wrong and make corrections. This fuzzy, anemic thinking during hyperthyroidism is a major obstacle in overcoming the disease. People get so weak that it's difficult to do the right things to get well.

Why do we get too much zinc and too little copper? Most meats are high in zinc and low in copper. People don't eat enough of the high copper foods. Also, many women are concerned about osteoporosis and are taking one of the popular calcium-magnesium-zinc supplements. Other people use zinc lozenges for colds. Taking zinc supplements without copper will create a copper deficiency.

Why do women become hyperthyroid more than men? Women seem to need more copper than men. It seems that many women first become hyperthyroid at the onset of menstruation as a teenager, during pregnancy or shortly after the birth of a child, or at menopause. Loss of blood during menstruation will deplete copper since copper is a part of hemoglobin. Copper can be depleted in a woman during pregnancy since the baby's needs come first. The mother loses a lot of minerals to the growing baby and as her body increases the amount of blood to meet both her and the baby's needs, she may become deficient in copper.

Another reason women may need more copper is that estrogen requires copper for its manufacture. Progesterone and testosterone require zinc for production. Excess zinc and too little copper causes too much progesterone and too little estrogen. Since progesterone seems to stimulate the thyroid and estrogen suppresses the thyroid, a high progesterone to estrogen ratio stimulates the thyroid too much. Chocolate craving seems to be a sure sign of copper deficiency and at the end of the menstrual cycle, as progesterone is peaking, women usually crave chocolate to increase the estrogen.

For a healthy person I believe that zinc and copper should probably always be taken together to avoid an imbalance and possible thyroid disease. My theory is that zinc and copper work as a pair (like calcium and magnesium or sodium and potassium) to regulate the thyroid (And I feel that it is quite likely that other minerals are involved also.) An excess of zinc with too little copper may lead to hyperthyroidism and too little zinc with too much copper may lead to hypothyroidism. I was taking zinc without copper when I became hyperthyroid.

This is just a theory at this point, but if it is correct you could think of zinc as the accelerator and copper as the brakes. If you have hyperthyroidism, it is because of a deficiency in copper--your brakes are gone! And if you have hypothyroidism (and plenty of iodine in your diet), it indicates that you are deficient in zinc (and other minerals like selenium)--your accelerator is not working.

So far I have not had one person with hyperthyroidism tell me that they were supplementing with copper (over .5 mg a day) either before or after getting ill. Several people told me that they were supplementing with zinc without copper (as I was). One woman with hypothyroidism said that she had been tested and had high copper levels. I think that hypothyroids (low thyroid output) have to increase their intake of zinc in relation to copper so that their thyroids will increase hormone production.

Wallach states that copper is essential for iodine utilization and is therefore critical for thyroid health. He says the optimum ratio of zinc to copper is about 8:1 (8 mg. of zinc for each 1 mg. of copper). Other sources have stated the optimum to be between 7:1 and 10:1. These ratios are for normal, healthy people. Hypers seem to have too much zinc and not enough copper, so supplementing with copper without zinc at the beginning seems to work the quickest to restore the proper zinc/copper balance and normal thyroid activity. A very small amount of zinc should be added when the energy level drops and then gradually increased.

I want to give you two lists: First, a list of all the supplements which I have taken during my recovery and which seem important to suppressing hyperthyroidism. Each supplement I take I've tested and re-tested

many times to make sure it makes me feel better.

Second, I want to give you a list of supplements I've experimented with many times and have concluded affect me adversely. I would recommend that if you are taking supplements to examine each one very carefully. Correct food choices are very important. It's possible that consumption of high zinc foods like meats and not enough copper foods like beans, shellfish, and liver may increase hyperT.

RECOMMENDED SUPPLEMENTS:

Copper (6-10 mgs. of amino acid chelated copper). I have experimented by taking up to 15 mg a day and am now taking 8 mg. I felt no difference between 8 and 15, but I recommend no more than 12 mg a day. If you only take one supplement make sure it's copper--I believe that it's the critical deficiency in hyperT.

Iron--works with copper and is essential for correction of anemia and hyperT. Take 18-36 mg a day, depending on your iron levels.

Sulfur--I took 2 tablets of MSM (methylsulfonylmethane, 500 mg.) per day. I think sulfur is essential for copper metabolism and seems to be involved in several inhibitory processes which may suppress thyroid function.

Silicon. From horsetail.

Boron (6 mgs. a day). I used Boron throughout my recovery and now believe it is vitally important in recovery from hyperT.

Trace Elements (An ionic trace element seems best, colloidal next best-- take the recommended amount).

Calcium/Magnesium (I've experimented with everything and found Solaray's Calcium/Magnesium Citrate works best for me--6 capsules provide 1000 mg of cal and 1000 mg of mag--most supplements give you more calcium than magnesium but I think the extra magnesium is important in controlling the rapid heart rate. The cal/mag seems to control the heart problems and prevent bone loss which happens in hyperT, but doesn't seem to help you get over hyperT. I took up to 36 capsules a day when I was really sick. Calcium is reported to decrease cellular sensitivity to thyroid hormone, while potassium increases sensitivity.

B-1 (200-500 mg a day). B-1 (thiamine) seems to be the critical B vitamin for copper utilization. A B-1 deficiency can cause inflammation of the optic nerve where it exits the back of the eye. B-1 and copper deficiencies may be the cause of eye involvement and protrusion in Grave's. My endocrine textbook says that the eye involvement is definitely not due to excess thyroid hormone.

B-2 (100-200 mg a day). Seems to assist copper and boron utilization and helps eye problems.

Niacin (100-200 mg a day). Seems to assist in copper utilization and helps hyperT. Start with a small amount (25 mg) and work up. Causes a harmless flush when you're deficient. Niacin is not replaced by niacinamide.

More protein--amino acids transport minerals to the cells, so proteins are vital. Try to eat the high copper proteins like beans etc. and eat less of the high zinc proteins.

More fats--to increase hormone production, especially estrogen, which is a thyroid suppressor.

Yogurt supplies vitamin K which may work with boron to produce estrogen and testosterone.

POSSIBLE NEGATIVE SUPPLEMENTS: Many of these essential nutrients may be in excess in hyperthyroidism can be reduced until the severe symptoms subside. Once the thyroid and heart rate slow, they may be re-introduced with caution. It's possible that other deficiencies may occur if these are discontinued for too long, so be careful.

Iodine (or Kelp) This is necessary for thyroid production, but it may be necessary to limit iodine intake until copper is built up to avoid serious hyper symptoms. Once copper is built up and the pulse drops (or if you go hypo), resume normal iodine intake.

Manganese--May need to be avoided for a long time. If your hair analysis shows low manganese, wait until you've been taking copper for awhile, and then take a small amount. Be cautious.

Selenium--Might be wise to not take this until copper is built up some, since selenium helps the T4 to t3 conversion. However, selenium is essential to thyroid health and should be taken as soon as it is tolerated.

Iron--Iron in excess is a copper antagonist and will deplete copper levels and make hyper symptoms worse. Take about 5 mg of iron for each mg of copper.

Zinc--This seems to be the major stimulator of the thyroid and should probably be avoided until the hyper symptoms subside and the heart rate comes down. However, zinc is a very necessary nutrient and needs to be supplemented in small but increasing quantities as you recover. Low energy can indicate that zinc is needed.

B-6--This seems to be the major B vitamin which increases utilization of zinc. Stopping intake of this slows down the utilization of zinc which is already in your body and seems to make a big difference in slowing the

thyroid.

Vitamin C (over 500-1000 mg a day) High amounts of C seem to aggravate hyperT, possibly by interfering with cal/mag and copper absorption.

Excess vitamin E (take 400 IU or less)

Multiple vitamin/mineral supplements--a problem because of zinc, iodine, and manganese.

B-Complex--a problem because the B-6 increases zinc utilization.

Ginseng (contains zinc and possibly stimulates progesterone production).

DHEA (seems to increase progesterone production.)

Pregnenelone (same as DHEA)

L-Carnitine

L-Arginine

L-Ornithine

Kotu Kola

Co-Q-10

Ginkgo Biloba

Testosterone stimulating herbs

Pine bark extracts like Pycnogenol and Phytonol

Grape seed extract

Garlic supplement

Any body building supplements or protein powders (milk and eggs contain growth hormone which may stimulate the thyroid)

Progesterone, especially synthetic forms such as Provera. I have not experimented with these but they seem to increase thyroid production.

Birth control pills--very often are synthetic progesterones.

FOODS TO AVOID UNTIL YOUR COPPER LEVELS INCREASE:

Fruits

Green leafy vegetables, like lettuce, spinach, chard, etc.

Iodized salt and foods with iodine.

Garlic and other high selenium foods.

All dairy products except butter--there is too much calcium and not enough magnesium in dairy products. Butter seems to be beneficial.

All white flour products--bread, pasta, etc. (may contain iodine as a preservative)

Once you have been taking copper for awhile, you should be able to resume consumption of these foods without a problem.

Many people have asked me if I know of any health professional who could help them with their hyperthyroidism. This nutritional approach to these diseases is completely new and it seems there are very few doctors, endocrinologists, or alternative practitioners who are aware of this approach. On the other hand, you need a doctor for anti-thyroid medications and blood tests so you can control the serious symptoms until your health recovers. Don't be mad at your doctor because he or she doesn't have the information to help you. They are doing the best that they can with the information that is available to them.

On the other hand be very careful. Doctors don't know about the connections between hormone supplementation and thyroid effects. Most don't know that Provera or other synthetic progesterones stimulate the thyroid and possibly cause hyperthyroidism. Also be aware that alternative health professionals may give incorrect information. I was told of one alternative practitioner who prescribed thyroid hormone or tyrosine (a thyroid hormone precursor) for hyperthyroidism, which makes the problem much worse. Your best strategy is to educate yourself. The people working at this site are devoted to research and sharing our

findings. This group effort is so much more powerful than working on your own, so be a part of the group.

My recommendation is that you take control of your disease yourself, get help from a nutritionist or nutritionally oriented doctor if you can find a good one and to work with our group at this site so that we and many others may benefit from our work. I hope to hear your input.

John L. Johnson

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HYPERTHYROIDISM

In Thyroid Theory (click on Hyperthyroidism Theory to the left.) you can read an outline of my theory of the causes of thyroid disease. This section is an elaboration of those ideas and a description of the deficiencies that lead to hyperthyroidism.

Here is a list of what I believe are the possible causes of hyperthyroidism (Graves' disease), in my "best-guess" rank order:

1. Inadequate [copper](#) in the diet.
2. Excessive [cadmium](#) intake such as from smoking or excessive consumption of green leafy vegetables.
3. Excessive [zinc](#) intake for the amount of copper intake. (Too high a zinc/copper ratio)
4. Excessive [aluminum](#) intake.
5. [Low vitamins](#) which metabolize copper.
6. [Low minerals](#) which work with copper such as iron and sulfur.
7. [Celiac disease](#) or other digestive deficiencies.
8. [Progesterone](#) use, including progesterone-based birth control pills.
9. High [estrogen](#) levels or estrogen replacement therapy combined with smoking, consumption of excessive green leafy vegetables, or inadequate copper intake.
10. Estrogen mimics from environmental sources including consumption of canned food.
11. [Lithium](#), sodium, and potassium imbalances.
12. Inadequate intake of protein or fat.

In hyperthyroidism, many nutrients are depleted. Most of the minerals become depleted because the high levels of thyroid hormone cause a hyper-metabolic state in which nutrients are used up at a high rate. Hyperthyroidism causes a catabolic state which is basically a process in which the body consumes its muscles and tissues to get raw materials to maintain life. People with hyperthyroidism can lose 20-40 pounds and a significant percentage of their muscle mass in a few weeks.

I believe that only a few nutrients are deficient which begins the process of hyperthyroidism and catabolism, but the disease itself causes the depletion of many more nutrients. All the nutrients, causal and consequential, need to be replenished.

The problem in correcting hyperthyroidism is that replenishing many of these deficient nutrients will worsen the condition. This may sound strange, but I've experienced it and seen it in many others. Once a key nutrient gets extremely deficient, taking other nutrients which work with that key nutrient cause that key nutrient to get used up and become even more deficient.

Using a shotgun approach to hyperthyroidism, in which nutrients are taken at random will most likely make the condition worse. Supplementation has to begin with the key nutrient to prevent it from getting even more deficient. This is the reason I call hyperthyroidism the "backward disease." Just about everything makes it worse, causing the person pursuing any of the commonly used nutritional correction strategies extreme frustration.

The two main minerals that seem to regulate not only the functioning of the thyroid but also the immune system are copper and zinc. Zinc acts as the stimulator to the thyroid and immune system and copper as the suppressor. It appears that when copper becomes deficient, both the thyroid and immune system will run out of control.

I believe that the main deficiency in hyperthyroidism is a copper deficiency. I've held this belief for two years since I recovered from hyperthyroidism by supplementing with copper and many other nutrients. I have been studying hyperthyroidism since that time and observing many people with hyperthyroidism improve once they have begun supplementing with copper. There have been no observations in those two years that have caused me to doubt this.

However, this copper deficiency can be the result of many different factors. Basically there seem to be three main ways to a copper deficiency to cause hyperthyroidism:

1. Inadequate copper intake.
2. Excessive intake of minerals which suppress copper absorption and utilization.
3. Inadequate intake of nutrients which work with copper.

To correct hyperthyroidism, since copper is usually the most deficient nutrient, starting the supplementation program with copper is usually the best approach. However, it's important to understand that it's possible to have hyperthyroidism even though there is adequate copper in the body. In this situation it appears that there are deficiencies of nutrients which assist copper metabolism.

Sometimes there is adequate copper in the body or even too much copper. At times there may be an excessive amount of copper seen in the hair and there is probably a buildup of copper in the liver and other organs. In some copper toxicity diseases such as Wilson's disease there is seen a buildup of copper in the cornea of the eye causing copper pigmented rings to be observable at the outer margin of the cornea. These rings are

called Kayser-Fleischer rings.

When copper builds up in bodily tissues like this, it appears that there is some reason that copper is not being utilized properly by the body. The reason might be that there is some genetic defect as it appears is the case in Wilson's disease, or it could be from a deficiency of some nutrients that are essential for copper metabolism.

Generally people with hyperthyroidism who have this inability to utilize copper have some schizophrenic characteristics to a lesser or greater degree. Several studies have shown that a relatively high percentage of patients diagnosed with manic-depressive schizophrenia also have hyperthyroidism. It seems that these two diseases share many of the same nutrient deficiencies.

While many people perceive schizophrenics as some type of strange people to be avoided, I consider schizophrenia as a disease condition that is probably the result of correctable nutritional deficiencies. It's just a symptom that is a clue to what is going wrong in the body.

However, these psychological problems can be an obstacle to correcting the disease. Mineral balances can cause disturbed cognitive processes and paranoia. These factors can prevent the person from perceiving a correct approach and taking steps toward solving the problem.

Unfortunately many health professionals will perceive these mental disturbances and inaccurately diagnose the disease. Many people who have these schizophrenic characteristics may perceive themselves to be a little different or even perceive that they have experienced a mental or emotional change. Consequently they may be primed to accept a misdiagnosis.

Typically when these people go to a doctor, the doctor will perceive these psychological problems and send them off to a psychiatrist who usually will wind up prescribing anti-psychotic drugs, rather than exploring the nutritional deficiencies that might have led to the condition. Many of these people continue to have hyperthyroidism, but a blood test to determine this is never done. Occasionally these people go online in an attempt to determine the source of their problems and will run into someone who will suggest that they get tested for hyperthyroidism. This is how they might find their way to this site.

I can usually see people of this type by their writing in emails. Usually they will not use any capital letters and write everything in the lower case, even using i when speaking of themselves. Sometimes the person will say "we" instead of "I" as if she were perceiving multiple personalities. Other times I see the emails written in all capital letters or other unusual styles.

If you perceive in yourself or you get feedback from others that you may have marginal or significant schizophrenic or manic-depressive behavior, and this is something that has not always been a part of you, then you should suspect that you have these problems because of nutrient deficiencies or imbalances. You are probably not deficient in copper, but are rather deficient in some other nutrients which are critical for copper metabolism. It's important to get a hair test to determine if you have high copper and if so, to proceed to a different nutritional correction program. See [Copper Overload](#).

Now let's look into the details of the list above of the most likely causes of hyperthyroidism:

1. Inadequate [copper](#) in the diet.
2. Excessive [cadmium](#) intake such as from smoking or excessive consumption of green leafy vegetables.
3. Excessive [zinc](#) intake for the amount of copper intake. (Too high a zinc/copper ratio)
4. Excessive [aluminum](#) intake.
5. [Low vitamins](#) which metabolize copper.
6. [Low minerals](#) which work with copper such as iron and sulfur.
7. [Celiac disease](#) or other digestive deficiencies.
8. [Progesterone](#) use, including progesterone-based birth control pills.
9. High [estrogen](#) levels or estrogen replacement therapy combined with smoking, consumption of excessive green leafy vegetables, or inadequate copper intake.
10. [Lithium](#), sodium, and potassium imbalances

At this point, I see that the most likely list of possible deficient nutrients in this case are: biotin, PABA, pantothenic acid (B-5), thiamine (B-1), riboflavin (B-2), and niacin (B-3). It's possible that there are toxic metals influencing this condition also, such as aluminum or cadmium (from smoking).

Copper metabolism is extremely complex. Copper performs many functions in the body and is therefore involved with many other nutrients to perform these functions. For copper metabolism to proceed correctly, many nutrients are needed. Deficiencies of any of a number of nutrients could result in a functional copper deficiency. Detailed information about how copper is involved in thyroidal and immune system functioning can be found under copper in the Nutrients and Toxics section under Minerals.

(To be continued.)

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HYPOTHYROIDISM RECOVERY STORY

I grew up in upstate New York with very little seafood on the table (a rich source of iodine). When I was in my early 20's I had dropped out of graduate school and was just laying around with no energy, wondering why. I started reading nutritional information and came across information about iodine and the thyroid gland.

My mother had hypothyroidism, as did her two sisters, and one of those sisters had three daughters, all of whom had thyroid problems: two of them hypo and one hyper. That's six close relatives with thyroid problems!

Thinking I might be deficient in iodine, I went to the drug store and got a kelp supplement and began taking it daily. My energy went up and I got myself to California and have been going strong ever since with only a few down periods (which I'm now viewing as deficiencies of other minerals.) Ever since then, every time I have gotten sick, I've pored over nutritional books until I've come up with an answer.

I eventually became a vegetarian and gradually took more and more supplements to improve my health and have always taken kelp, usually 4-10 tablets a day. Iodine can be lost by sweating and a lot is lost in exercise so I've always taken a lot more than the one kelp tablet recommended. I've always exercised a lot and had lots of energy for work and play. Whenever I got sick I would eat fruit only, go on a raw food diet, or if necessary, fast.

In July of 1985 I started feeling heart irregularities for about a week until one day when I was taking my family in the van to go bicycle riding when I started feeling some pain in my heart and felt really sick. I stopped and when I got out of the van to rest I passed out. That began a long mysterious sickness which lasted on and off many years. My wife drove me home where I found relief only after taking an enema and drinking grapefruit juice.

Over the next few months, I would have "attacks" where my heart rate would slow, my blood pressure plummet and I would feel like I was going to pass out. I discovered that drinking a large quantity of fresh-squeezed lime juice and/or taking a lime or lemon juice enema would be the only way to feel better.

Although I had always avoided doctors like the plague, I went to a nutritional doctor who ordered a hair analysis and blood tests and waited for the results. Before my appointment a month later (for the hair results), I went on a scheduled family camping trip, hoping that would help me recover. I kept getting worse and by the time I returned home I was really sick.

When I returned to the doctor, the tests showed I was very deficient in B-12, zinc, chromium, selenium, and slightly deficient in copper. I also had low thyroid output and had candida, a yeast infection. The doctor put me on capristatin for the candida at the end of July on the theory that candida was the major problem, but my health continued to deteriorate. In September he prescribed various vitamins and B-12 injections, which helped a little but I was still in bad shape.

I felt so bad that as an experiment I got some Armour thyroid hormone from my mother and tried that. That really made a big difference and helped a lot. In October, the doctor prescribed zinc, selenium, and chromium and gave me a prescription to continue the thyroid hormone.

Within a few months after starting the mineral supplements which included zinc and selenium, I noticed a significant change one day. A couple hours after breakfast when I took my supplements and thyroid hormone I began sweating, trembling, and feeling hot. It was very unusual because most of the time I felt cold from the hypothyroidism. After a few hours of thinking that I was dying, I realized that my thyroid gland had probably recovered. Within a day of stopping the thyroid hormone, I felt relatively good! After months of taking the supplements, my thyroid recovered very suddenly.

The next summer (1986) I had another period of the same attacks which went on for a year until the summer of 1987. I fasted several times for 8-10 days, ate raw foods, eliminated nearly every potential environmental toxin I might be exposed to, but nothing seemed to help. I went to several doctors, all of whom failed to find anything wrong with me. I seemed to be getting allergic to more and more things and had the feeling that I was being poisoned. I felt I was being poisoned by the whole environment and everything I ate. I had a very bad case of multiple chemical sensitivity (MCS).

I gradually eliminated everything from my diet that adversely affected me and one day realized that there were only four foods that agreed with me: raw potatoes, grapefruit, lemons, and limes. I knew I was in really big trouble. My weight had gone from 175 to 142. I was going through attacks when I would feel terrible and have heart problems and the only thing that would stop it was a massive drink of fresh squeezed lime juice and water. It was so strange and despite poring over nutritional books I could not figure out what was going on.

One day I found a book about candida (which I was still suffering from) and silver amalgam fillings. The book described how mercury toxicity from dental fillings can cause candida and other symptoms of mercury toxicity. The descriptions of mercury poisoning seemed to match what I had been experiencing and I did

have 12-15 silver fillings so it made sense to me. I decided to have my fillings removed.

I found a dentist who specialized in replacing mercury fillings and had them replaced with a plastic composite. He removed a quarter of the fillings (one quadrant) at a time and for two days after each session I would feel really terrible, but would gradually improve to the point where I felt better than before. Two days after the last fillings were removed, I felt significantly better. It seemed that getting rid of the mercury made a big difference for me.

In 1998 I tried to put all my medical records together in an attempt to unravel the whole mystery of my years of illness. I went back over dental records and discovered that about a week before my first symptoms appeared in July of 1985 when I fainted, I had had a large amalgam filling put into one of my molars. The next July (1986), just a week before my relapse, a dentist had put in two amalgam fillings. This was as much proof as I could want: both year-long bouts of sickness began within days of getting mercury fillings put into my teeth.

I have pieced together what happened. Selenium is an essential potent anti-oxidant which protects the body from free radical damage but it also has an important function in preventing mercury from damaging the body. Selenium and mercury combine together and the combination is eliminated from the body. Without selenium, mercury poisons the body. As my hair analysis showed, I was deficient in selenium and therefore the mercury which was released from the new fillings was not properly eliminated from my body. Mercury removal is a top priority of selenium and this caused a severe deficiency of the selenium. Selenium is essential for both the production of thyroid hormone and for the conversion of the T4 hormone that the thyroid makes into the T3 hormone that the cells use. My hypothyroidism was the direct result of a combination of too little selenium and too much mercury from dental amalgam fillings. This is why the hypothyroidism ended after I had the mercury removed from my body and I began supplementing with selenium.

It is also possible that a deficiency of zinc may have contributed to the hypothyroidism. I've read that selenium and zinc perform many similar functions and can spare each other. A selenium deficiency can also cause zinc to be used fulfilling many functions that selenium should perform. This can cause zinc to get depleted. My theory is that zinc and copper work together to regulate the thyroid. A deficiency of zinc leads to hypothyroidism and a deficiency of copper (with excessive zinc) leads to hyperthyroidism.

Another mineral that I feel is very important to combat hypothyroidism is chromium. Broda Barnes, who is an MD and an expert on hypothyroidism, feels that diabetes and hypothyroidism share so much in common that they might be considered the same disease. Wallach states that diabetes is a disease caused by chromium and vanadium deficiencies and therefore these two elements might be critical to prevent hypothyroidism.

While hypothyroidism causes people to put on excess fat, chromium has been shown to cause people to lose fat, even if they don't exercise. Perhaps the mechanism is the thyroid gland, the regulator of the metabolic rate? A chromium deficiency seems to cause the thyroid to slow down.

Once a couple years later when I was very deficient in chromium I felt like I was experiencing hypothyroidism. Supplementing with chromium restored my ability to handle sweet foods like fruit and increased my energy significantly. I think it's a supplement all people with hypothyroidism should take and may one day be proved to be essential for thyroid function.

I was very slow about taking a chromium supplement. At first I would feel terrible after taking chromium and and I would discontinue it. I struggled for years to find a chromium which didn't make me feel worse and now use chromium picolinate. Now I think I may have been in error to discontinue the chromium supplementation and feel that perhaps when you are very deficient in a mineral you may experience feeling very sick initially, but gradually you'll feel better than ever. Chromium, in particular, is involved in producing many detoxification products that the body requires. Replenishing chromium after a long deficiency could result in a rapid elimination of toxins which would be associated with discomfort.

Although I've studied nutrition for 27 years, most of my studies centered on vitamins. I rarely considered minerals, feeling that our foods contain lots of minerals. Lately, however, I've realized that the plant based diet I've been trying to live on for years may be very deficient in minerals. Farmers fertilize their fields with NPK (nitrogen, phosphorus, and potassium) but rarely with trace element rich fertilizer. Consequently, although the produce and grains look great, they are very deficient. As years go by, the situation only worsens.

Now I believe that to maintain excellent health, we have two options: one, widening the variety of foods we eat to include more meat (especially liver, which is the body's mineral storehouse), seafood (especially the bottom-feeding shellfish we've been educated to avoid, like oysters, clams, crabs, and lobsters), and foods grown on volcanic soil; or educating ourselves about minerals and trace elements and making sure we get adequate amounts of the 60 or so essential ones daily. I plan on doing both.

If you start taking the mineral supplements I recommend to get your thyroid working properly again, I suggest that you don't reduce your thyroid hormone first. Wait until you feel the hot, sweaty, trembling feeling you probably already know is from too much hormone. Then gradually reduce the hormone until you feel right again. When I went through that, I was taking only 30 mg of Armour thyroid a day and stopped it all immediately. You may be different.

Some people have written to me wanting a natural alternative to Synthroid, a synthetic thyroid hormone. Dr.

Julian Whitaker wrote in his newsletter "Health & Healing" in December, 1997 about this. He states that, "natural thyroid...is desiccated porcine (pig) thyroid gland and contains all the gland's hormones and components, versus the more popular levothyroxin (Synthroid), a synthetic version of only one of the thyroid hormones, T4."

One natural thyroid hormone is Armour (the meat-packer), which is what my mother uses. She had a lot of problems when a doctor tried to switch her to Synthroid. Many people seem to feel that Armour is better although a few do better on Synthroid or levothyroxin.

Also of importance are a class of foods called goitrogens, which interfere with the thyroid's metabolism and can cause goiter when consumed in large quantities. They include nitrates, broccoli, cabbage, brussel sprouts, and some raw nuts. It's a good idea to avoid eating a lot of these.

The hormones progesterone and estrogen seem to affect the thyroid. Excess estrogen seems to suppress the thyroid, while progesterone seems to stimulate thyroid function. Birth control pills may have synthetic estrogen, synthetic progesterone, or both. If you are taking estrogen replacement therapy or birth control pills with estrogens, these may be suppressing your thyroid function.

Zinc seems to promote more progesterone production, while copper stimulates estrogen production. Both hormones are necessary, but in hypothyroidism it seems that there is a progesterone deficiency. Supplementation with these recommended nutrients should bring the hormones into balance and restore normal thyroid function.

Here is a list of supplements I feel were important in healing my thyroid gland and enabling me to get off of thyroid hormone:

Multiple vitamin/mineral. It's easiest to get a good multiple and then add the necessary nutrients as necessary to get the amounts listed below.

Zinc (30-100 mg/day) There are various forms but I find the citrate or picolinate work best for me. Zinc can give you more energy since it stimulates the thyroid and some people take up to 100 mg a day to get more energy. Don't take more than 100 mg a day. Always take zinc in the morning (at the end of breakfast so you don't get nausea) Taking it at suppertime may keep you awake at night. If you start having trouble sleeping or have any rapid heart beat, take less zinc. Always take copper with zinc and eventually you'll want to get your zinc/copper ratio close to the ideal of 8:1 (zinc to copper). Taking excessive amounts of zinc without copper may cause hyperthyroidism. Phytates in grains and beans interfere with zinc absorption. You may want to limit your consumption of whole grains and beans (especially soybeans) until your thyroid function is normal. Zinc is involved in many enzymes and it is reported to be necessary for conversion of T4 to T3.

Copper (2 mg/day) I use a chelated copper, but other types should be fine. Take copper at the end of a meal because it will cause nausea if taken on an empty stomach. If you already have a sufficient amount of copper in your body, additional copper may slow your thyroid down more and you don't want that. If you feel that happening, stop the copper for awhile and let the zinc get built up and then resume the copper. Copper is the brake for your thyroid, so you don't want your thyroid to get going without having a sufficient amount of copper in your body. So start with 1 mg a day and work up to 2 mg when you can (after the zinc gets built up). Once your thyroid starts working properly, you may want to increase the copper to 4 mg and decrease the zinc to maintain the optimum 8:1 zinc/copper ratio to ensure that you don't get hyperthyroidism. Copper is also essential for iodine absorption.

Selenium (200-400 mcg/day--don't overdo) I use a sodium selenite (yeast free). Selenium is supposed to be very beneficial for hypothyroidism. I believe this was crucial in stopping the mercury poisoning which may have put me into hypothyroidism. If you have any silver amalgam fillings, this is very important.

Chromium (200 mcg/day of chromium picolinate-don't overdo). This is very important in insulin formation which will stabilize blood sugar. Chromium is important to reduce body fat without losing muscle. Chromium deficiency leads to both hypothyroidism and diabetes.

Iodine in the form of Kelp (start with one tablet and work up to not more than 10 tablets a day--each tablet contains about 225 mcg of iodine). This is crucial. Iodine is excreted in sweat so supplement accordingly for exercise and in hot weather. There are also trace elements in kelp which are important. If you are very deficient in copper, you may experience hyper symptoms from taking kelp. Stop it until your copper gets built up and then try again very cautiously.

B-12 Get tested for a deficiency. If you've been a vegetarian or close to it for years, you could be very deficient. Without B-12 (cobalt) everything falls apart (anemia, etc.) I had to have shots to replenish my body's stores. This really helped.

Calcium/Magnesium People vary tremendously in how much they need and how well they absorb different forms. I've been using a citrate lately and it seems to absorb well.

Manganese (5 to 10 mg a day). An essential trace element to make thyroid hormone.

Iron (10-18 mg a day) Iron is important in thyroid hormone production.

Trace elements (follow directions) Try to find an ionic form of trace elements, but colloidal is better than nothing.

Vitamin E. (400 IU natural with mixed tocopherols). Assists progesterone production and thereby stimulates the thyroid. Don't take more than 400 IU per day, and take it in the morning. If you've never taken E before start with no more than 100 IU per day.

B-complex-50 mg. Each B vitamin seems to facilitate the utilization of specific minerals. Zinc is facilitated by vitamin B-6, so you may want to try extra B-6 to increase zinc metabolism.

Niacin (100 mg a day). B complexes and multiples have niacinamide, which is a synthetic niacin. I feel that niacin addition is essential. Niacin seems to increase serotonin production, assists mineral metabolism, and increases the production of sex hormones which stimulate the thyroid.

Seafood--Essential to provide protein and essential trace elements. Minerals are transported to the cells by amino acid transporters, so without sufficient protein in the diet, minerals may not get to the cells.

John

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MEDICAL TREATMENTS FOR HYPOTHYROIDISM AND HASHIMOTO'S THYROIDITIS

SYNTHROID OR LEVOTHYROXINE SODIUM

The basic medical treatment for hypothyroidism is the administration of replacement thyroid hormone. Most doctors will insist on prescribing Synthroid which is a brand name for levothyroxine sodium. This is the monosodium salt of the levo isomer of the thyroid hormone thyroxine (T4). Therefore Synthroid or other brands of levothyroxine sodium will provide the same chemically identical hormone that our thyroid hormones make.

While there are other manufacturers of levothyroxine sodium, doctors seem to insist on prescribing Synthroid which is much more costly. My suspicion is that the doctors are getting kickbacks, perhaps in the form of free trips (which is a form of kickback in the pharmaceutical business), for prescriptions written for Synthroid. (Someone could look into this and report back.)

Levothyroxine sodium will work for many people with hypothyroidism and will alleviate some of the symptoms. However, many hypothyroids will not respond well to levothyroxine sodium.

In my experience, most hypos are deficient in selenium and zinc. These two minerals are critically important for converting the body's supply of thyroxine (T4) into triiodothyronine (T3), which is the hormone that the body uses at the cellular level. Thyroxine is known as a "prohormone" because the body has to convert it into another hormone for use.

Therefore taking levothyroxine sodium or Synthroid is the same as taking a prohormone. The body has to convert it into the active hormone (T3) for the effects to be felt. If the hypothyroidism is due to a breakdown of the conversion of T4 to T3, the person will feel little benefit from taking T4 (thyroxine or Synthroid).

ARMOUR THYROID HORMONE

Another way to get thyroid hormone is to extract it from animals slaughtered for meat consumption. The packing company Armour produces such a hormone and the hormone is also called Armour. The advantage of Armour is that in addition to T4 it contains some T3 which has already been converted from the T4. Also there are some references in the literature to other forms of thyroxine, such as T7 (there might be T5 and T6 also). I don't know if these are very important, but there is the possibility that they have some minor functions, if they exist at all).

Hypos who are suffering from an inability to convert T4 to T3 (and these persons usually also have low production of T4) benefit from Armour more than from Synthroid. More than likely Synthroid might be found just as beneficial as Armour if sufficient amounts of selenium and zinc are provided through supplementation, but it could take a period of time (days or weeks) to replenish these minerals if they are seriously depleted.

Some people might object to the use of Armour for other reasons. There was a time when the potency of Armour varied, but it seems as though the company has corrected that problem. Also, some people object to taking something from animals but that is just a fear and I don't see any justification for that fear.

Overall, I think that hypos will do better taking Armour rather than Synthroid or another manufactured form of levothyroxine sodium.

HOW MUCH HORMONE?

Many people feel that since they have to take thyroid hormone then their thyroid glands must be "shot." Doctors do their best to persevere this myth by telling patients that their thyroid has "burned out" or will burn out. I think this is nonsense.

As an approximation, our thyroid glands produce about 300 mcg of hormone a day. Therefore the thyroid gland of a hypo taking 100 mcg of replacement hormone a day is producing about two thirds of the hormone that is needed. Very, very rarely will you see a person taking over 200 mcg per day. As you can see, most hypos thyroids are producing more than half of the thyroid hormone needed. To me this is not "burned out."

I am not the only person with the belief that by providing the body with the proper nutrients the thyroid will be able to produce all the thyroid hormone needed. It's not a matter of taking a "dead" thyroid and bringing it back to life. It's a matter of taking a thyroid that is under producing and getting it to produce more. It's possible and people are doing it.

Some people wonder if they take less hormone than they need will that stimulate the thyroid to produce more hormone. I tried this when I was hypo and also looked into this. I've seen no evidence that this strategy will work. I believe the thyroid gland is doing the best that it can and will produce more hormone when it has the raw materials to do so.

WHEN YOU THYROID RECOVERS

If you take the supplements that your thyroid gland needs to produce hormone you may experience a sudden increase in the production of thyroid hormone. I experienced this in my recovery from hypothyroidism.

I had recently had my silver amalgam (mercury) filling replaced and was supplementing zinc and selenium along with other supplements. One morning about an hour after breakfast when I took my Armour hormone and my nutritional supplements, I got very hot, sweaty, and shaky. After a short period of thinking that I was really sick or dying, I reasoned that my thyroid gland may have recovered. I stopped taking thyroid hormone and within a couple days I was feeling much better.

While thyroxine has a half life in the body of about 7 days, triiodothyronine (T3) has a half-life of about 10 hours. This means that if your thyroid suddenly starts producing hormone or your T4 to T3 conversion suddenly increases, you could have high levels of T3 for a day or two, but these levels will soon return to normal.

There have been other members of the group who have experienced this sudden increase in thyroid production who have gone through this "hyper episode." That period can be frightening but it passes. The best strategy is to discontinue the replacement hormone to see if it passes. You can call your doctor to tell him or her what you've done. You may find that your thyroid gland has completely recovered and you no longer need replacement hormone or you may find that you need to resume replacement hormone at a lower dosage.

If you have any questions, just post a message on the Bulletin Board.

Studies:

From Dr. Mercola's site at www.mercola.com:

NEJM Study Proves Armour Thyroid Better Than Synthroid

Patients with hypothyroidism show greater improvements in mood and brain function if they receive treatment Armour thyroid rather than Synthroid (thyroxine). Hypothyroidism, where the gland has ceased to function or been removed, is usually treated with daily doses of Synthroid. But the researchers found that substituting Armour thyroid led to improvements in mood and in neuropsychological functioning.

Not all tissues that need thyroid hormone are equally able to convert thyroxine to triiodothyronine, the active form of the hormone. But most patients with hypothyroidism (reduced thyroid function) are treated only with thyroxine. On 6 of 17 measures of mood and cognition -- a catchall term that refers to language, learning and memory -- the patients scored better after receiving Armour thyroid than after receiving Synthroid. No score was better after Synthroid than after combination treatment. The authors also detected biochemical evidence that thyroid hormone action was greater after treatment with Armour thyroid. The patients who were on Armour thyroid had significantly higher serum concentrations of sex hormone-binding globulin

The New England Journal of Medicine 1999;340:424-429, 469-470.

COMMENT: Extracts of animal thyroid tissue, first used in 1892, contained both thyroxine and triiodothyronine (Armour thyroid) and were the only available treatment for hypothyroidism for some 50 years. Because of concern about their variable potency, these extracts have been considered obsolete for some time by all but a few natural prescribers. This is a MAJOR article. I did not realize that natural therapies would penetrate this far this quickly. I am very surprised that this was published in NEJM. If one reads the editorial, you will find that it recommends that patient NOT switch from Synthroid to Armour thyroid because more research needs to be done and "the majority of patients taking Synthroid "have no complaints about their medication." If your doctor or endocrinologist refuses to give you Armour thyroid instead of Synthroid, you can use this article to show him that it is indeed better. Synthroid (thyroxine) is RARELY ever the best choice for hypothyroid patients.

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IODINE

Iodine is essential for the formation of thyroid hormone and a deficiency will cause goiter and primary hypothyroidism. In countries where iodine is deficient in the soil, rates of hypothyroidism and goiter from iodine deficiency are very high. In developed countries, however, because iodine is added to salt, iodine deficiencies are rare. It's possible to get iodine deficient, but it takes work. You would have to eat non-iodized salt, stay away from processed foods, and not eat iodine rich foods like seafoods.

However, there may be interactions between eating certain foods and marginal iodine deficiency which could lead to goiter and hypothyroidism. The following study indicates that this might happen with high consumption of soybeans (or other beans) which are known to be high in copper.

This study shows that both defatted soybean consumption and iodine deficiency decrease thyroid hormone production and cause an increase in thyroid gland size. However there is a very significant synergism between soybean consumption and iodine deficiency. Look at the thyroid gland weights. While iodine deficiency caused a doubling of thyroid gland weight (from 8.4 to 15.5), iodine deficiency combined with soy intake caused the weight to nearly increase 10-fold!! (from 8.4 to 81.7).

Carcinogenesis 2000 Apr;21(4):707-13

Dramatic synergism between excess soybean intake and iodine deficiency on the development of rat thyroid hyperplasia.

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The effects of defatted soybean and/or iodine-deficient diet feeding were investigated in female F344 rats. Rats were divided into four groups, each consisting of 10 animals, and fed basal AIN-93G diet in which the protein was exchanged for 20% gluten (Group 1), iodine-deficient gluten (Group 2), 20% defatted soybean (Group 3) and iodine-deficient defatted soybean (Group 4). At week 10, relative thyroid gland weights (mg/100 g body wt) were significantly ($P < 0.01$) higher in Groups 2 (15.5 \pm 1.3) and 4 (81.7 \pm 8.6) than in Group 1 (8.4 \pm 2.0) and pituitary gland weights (mg/100 g body wt) were significantly ($P < 0.01$) higher in Groups 3 (9.1 \pm 0.6) and 4 (9.7 \pm 1.5) than in Group 1 (6.5 \pm 1.5). Serum biochemical assays revealed thyroxine to be significantly ($P < 0.05$) lower in Groups 2 and 4 than in Group 1. On the other hand, serum thyroid-stimulating hormone (TSH) was significantly ($P < 0.01$) higher in Groups 3 and 4 than in Group 1. This was particularly striking for TSH (ng/ml) at week 10 in Group 4 (126 \pm 11) as compared with Groups 1 (4.36 \pm 0.30), 2 (4.84 \pm 0.80) and 3 (5.78 \pm 0.80). Histologically, marked diffuse follicular hyperplasia of the thyroid was evident in Group 4 rats. Proliferating cell nuclear antigen labeling indices (%) were significantly higher ($P < 0.05$) in Groups 2 (4.8 \pm 2.5) and 4 (13.2 \pm 1.1) than in Group 1 (0.4 \pm 0.5). Ultrastructurally, severe disorganization and disarrangement of mitochondria were apparent in thyroid follicular cells of Group 4. In the anterior pituitary, dilated rough surfaced endoplasmic reticulum and increased secretory granules were remarkable in this group. Our results thus strongly suggest that dietary defatted soybean synergistically stimulates the growth of rat thyroid with iodine deficiency, partly through a pituitary-dependent pathway.

Here is the rough file:

Eur J Endocrinol 2000 Oct;143(4):485-91

Comparative study of thyroid function and types of thyroid dysfunction in two areas in Denmark with slightly different iodine status.

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OBJECTIVE: The pattern of thyroid dysfunction seems to depend on the iodine status of the population. Prevalence of thyroid dysfunction could be a parameter to consider when evaluating iodine deficiency disorders in a population. **DESIGN:** Comparative cross-sectional investigation in two regions in Denmark with marginally different iodine excretion. **METHODS:** A random selection of 4649 participants from the Civil Registration System in Denmark in age groups between 18 and 65 years were examined. Thyroid dysfunction was evaluated from blood samples and questionnaires, and compared with results from ultrasonography. **RESULTS:** Median iodine excretion was 53 microg/l in Aalborg and 68 microg/l in Copenhagen. Previously diagnosed thyroid dysfunction was found with the same prevalence in the regions. Serum TSH was lower in Aalborg than in Copenhagen ($P=0.003$) and declined with age in Aalborg, but not in Copenhagen. Not previously diagnosed hyperthyroidism was found with the same overall prevalence in the regions, but in age >40 years hyperthyroidism was more prevalent in Aalborg (1.3 vs 0.5%, $P=0.017$). Not previously diagnosed hypothyroidism was found more frequently in Aalborg (0.6 vs 0.2%, $P=0.03$). Hyperthyroidism was more often associated with macronodular thyroid structure at ultrasound in Aalborg and hypothyroidism was more often associated with patchy thyroid structure in Copenhagen. **CONCLUSIONS:** Significant differences in

thyroid dysfunction were found between the regions with a minor difference in iodine excretion. The findings are in agreement with a higher prevalence of thyroid autonomy among the elderly in the most iodine-deficient region.

J Clin Endocrinol Metab 2000 Apr;85(4):1513-7

The changing incidence and spectrum of thyroid carcinoma in Tasmania (1978-1998) during a transition from iodine sufficiency to iodine deficiency.

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Exposure to ionizing radiation, changing levels of iodine nutrition, and increased pathologic diagnosis of clinically unimportant thyroid neoplasia have all been proposed as explanations for a worldwide rise in the incidence of thyroid carcinoma (TC) over the past 6 decades. Tasmania is geographically an area of endemic iodine deficiency. In this report, we describe the spectrum of TC in a population averaging 450,000 persons during a 21-yr period that spans the communities transition from iodine sufficiency to iodine deficiency after discontinuation of universal iodine prophylaxis in the mid 1980s. The Tasmanian Cancer Register was used to ascertain all cases of TC diagnosed in Tasmania between 1978 and 1998. Histopathological and demographic data were reviewed. A total of 289 cases of TC were identified. Papillary TC (PTC), follicular TC, medullary TC, and other species accounted for 62%, 23%, 4%, and 11% of cases, respectively. The age standardized incidence rate for total TC increased from 2.45 to 5.33 per 100,000 for females and 0.75 to 1.76 per 100,000 for males between 1978 and 1984 and 1992 and 1998, respectively. A rise in the incidence of PTC by 4.5-fold ($P < 0.05$) in females and 2.1-fold in males (not significant) was the dominant change over this period. In parallel, the proportion of follicular TC relative to PTC fell from 0.35 to 0.17 during these years ($P < 0.05$). The rise in PTC incidence was, in part, due to an increase in the occurrence of tumors 1cm or less in diameter. Nonetheless, a 3-fold rise in incidence of larger lesions was also observed during the study period. Forty-three (24%) PTC cases had multifocal disease, 17 (40%) of whom had bilateral tumors. Familial (autosomal dominant) PTC was identified in nine (5%) total PTC cases. Prior studies have linked iodine prophylaxis to a rise in the proportion of differentiated TC, particularly PTC. Our data suggest a complex relationship between iodine nutrition and thyroid tumorigenesis. Factors such as a long latency between changes in iodine nutrition and thyroid tumorigenesis, a dose threshold for the effect of iodine nutrition on thyroid tumorigenesis, and an interaction between iodine nutrition and thyroidal sensitivity to ionizing radiation may all play a role.

Iodine deficiency leads to a decrease in the activity of deiodinase enzyme and consequently to lower levels of T3. [selenium--high intake does not lead to high D-I.doc](#)

"Inhabitants of many severe endemic goiter areas have low serum T4 and high circulating TSH, despite normal levels of T3. This situation may be produced experimentally chronically feeding rats a low iodine diet (LID). We fed rats a Remington-type LID and gave them 1% NaClO₄ in their drinking water for 2 days. After this, the animals were divided into three groups. One group was fed LID, supplemented with 5 micrograms I/rat.day and was used as the control group. Another group was fed LID alone. The third group was fed LID and given 1% NaClO₄ to drink. The latter treatment was used to induce severe hypothyroidism. Animals were killed 1, 2, 3, and 5 weeks after the onset of these treatment schedules. The following measurements were made on some or all groups of animals: body and thyroid weights; thyroidal I content; soluble labeled iodoprotein profile; thyroidal labeled iodoamino acid distribution pattern; plasma T4, T3, and TSH; pituitary GH content; and liver intramitochondrial alpha-glycerophosphate dehydrogenase and cytosolic *malic* enzyme activities. T4 and T3 concentrations were also measured in liver nuclei of the animals killed 5 weeks after the onset of treatment. As assessed from various indices of thyroid function, the LID rats became iodine deficient, although not as markedly as those given LID and ClO₄⁻. The plasma T4 decreased to undetectable levels, and plasma TSH increased, whereas circulating T3 remained normal throughout in the LID rats. In rats given LID and ClO₄⁻, plasma T4 decreased sooner than in rats given LID alone; plasma T3 levels also became undetectable, and TSH increased more markedly and sooner than in rats given LID alone. As measured at the end of 5 weeks of treatment, pituitary GH content, and liver alpha-glycerophosphate dehydrogenase and *malic* enzyme activities were lower in rats given LID than in the euthyroid LID- and I--treated controls. They were not, however, as markedly reduced as in the severely hypothyroid LID- and ClO₄⁻-treated rats. In spite of normal plasma T3 levels, the concentration of T3 in liver nuclei of the rats given LID alone was significantly lower than that of the LID- and I--treated controls. The results show that the thyrotrophs, somatotrophs, and livers of rats given LID alone are not like those of euthyroid rats despite normal circulating T3 levels. In iodine-deficient rats, there is a discrepancy between the measured indices of thyroid hormone action in the liver and the circulating T3 level, but not between biological activity and liver nuclear T3 concentration. It remains to be seen whether the same is true in the anterior pituitary." [iodine deficient rats.doc](#)

Three patients with subclinical hyperthyroid goitre, women aged 63, 72 and 75 years following intravenous administration of an iodinated contrast medium developed hyperthyroidism with a marked rise of the concentration of free T4. Thyreostatic agents were unsuccessful in two patients, the third was left untreated. Hyperthyroidism improved spontaneously in all three. Iodine-induced hyperthyroidism is rare and is usually encountered in patients with a pre-existent autonomous thyroid function. Treatment of iodine-induced hyperthyroidism is essentially exclusively symptomatic. Prophylaxis with **sodium** perchlorate should be considered in cardiac patients with a goitre and a subnormal level of thyroid-stimulating hormone (TSH). [iodine induced hyperT.doc](#)

The high prevalence of goiter and hyperthyroidism with low prevalence of hypothyroidism probably resulted from the combined effects of food goitrogens and iodine **deficiency** in Ethiopia, with the latter playing only a minor role. Neither factor was in effect after arrival in Israel. Genetic and hormonal factors may contribute to the low prevalence of both goiter and hypothyroidism in the adult males. In view of the high prevalence of hyperthyroidism, iodine enrichment is not recommended for Ethiopian immigrants. [iodine enrichment in goitrous people can lead to hyperT.doc](#)

In areas with relatively high iodine intake, the incidence rate of hypothyroidism is several-fold higher than that of **hyperthyroidism**. Recently, we found a similarly high prevalence rate of subclinical hypothyroidism compared with **hyperthyroidism** in a high iodine intake area, while a relatively low prevalence of subclinical hypothyroidism was observed in a low iodine intake area. In the present study we compared the incidence rate (newly diagnosed in primary care and at hospital) of overt hypothyroidism with that of **hyperthyroidism** in a well-defined geographical area in Jutland, Denmark, with an iodine intake around 60 microg/day. The number of personsxyears studied was 569,108. Data on **hyperthyroidism** have been published previously. The overall incidence of hypothyroidism was 13.5/100,000 per year (F/M 22.9/3.6), **hyperthyroidism** 38.7/100,000 per year (F/M 63.0/13.0). The incidence of hypothyroidism was steadily increasing with age up to 80/100,000 per year in subjects older than 70 years of age, but apart from congenital hypothyroidism it was lower than that of **hyperthyroidism** at all ages. The majority of patients (79%) was diagnosed to have spontaneous autoimmune hypothyroidism (16% with goiter, 84% with no thyroid visible or palpable). In conclusion, in an area with moderately low iodine intake, hypothyroidism was considerably less common than **hyperthyroidism**. This is in contrast to findings in high iodine intake areas. The iodine intake of an area seems to be of major importance for the pattern of thyroid disorders observed. [iodine low in soil--hypoT low and hyperT high.doc](#)

Groups of 6-wk-old male F344/NCr rats received a single i.v. injection of either vehicle or N-nitrosomethylurea (Cas: 684-93-5) (MNU) at a dose of 41.2 mg/kg body weight. Two wk later, groups of rats were placed on iodine-deficient, iodine-adequate, or commercial (Wayne Lab Blox) diets, or one of these diets and without previous MNU injection. Animals were sacrificed at either 52 or 77 wk, or when they became moribund. Carcinogen-treated rats on the iodine-deficient diet for up to 52 wk had significantly increased thyroid gland weights and increased incidences of both thyroid follicular cell carcinoma (90%) and diffuse pituitary thyrotroph hyperplasia (90%) at 52 wk. The majority of the follicular carcinomas were transplantable and invasive into the mammary fat pad of weanling F344/NCr rats. No other tumors induced by MNU were affected by the iodine-deficient diets. Rats fed the iodine-deficient diet without MNU injection had a 40% incidence of thyroid follicular adenomas at 52 wk and 60% at 77 wk, and a 10% incidence of follicular carcinomas at 77 wk. **Thus this experiment provided evidence that the iodine-deficient diet is a potent promoter of thyroid tumors initiated by MNU and carcinogenic by itself.** In addition, pituitary tumors were found in 29 of the 58 rats treated with the carcinogen alone, compared to only 3 of the 20 rats in the control groups. The vast majority of these pituitary tumors contained prolactin that was demonstrable by the **avidin:biotin:peroxidase complex immunocytochemical technique**. [iodine deficiency contributes to thyroid cancer.doc](#)

About 90% of all functional thyroid autonomies (FTA) are euthyroid for a prolonged period of time. It is estimated that more than 10% of goiter patients in iodine **deficient** regions and less than 10% in iodine rich areas have evidence of FTA. After the age of 40, the risk of hyperthyroidism decompensation gradually increases. This risk rises with increasing thyroid volume, nodularity and patient age. In the elderly, hyperthyroidism also occurs in the absence of goiter. After decades of iodine **deficiency**, especially the intake of unphysiologically high iodine concentrations may result in increased frequencies of hyperthyroidism. In iodine **deficient** regions, almost half of all cases of hyperthyroidism are FTA related. Following elimination of iodine deficiency, the rate of hyperthyroidism may be reduced below 10%. This will not affect the prevalence of immunogenic hyperthyroidism. [iodine can cause hyperT in iodine deficient populations.doc](#)

JJ: There is literature suggesting that an iodine deficiency can lead to thyroid cancer. Research this because hyperts who control their hyperT by iodine restriction might be subject to this risk.

A cross-sectional study in two stages consisted of healthy children to assess the effect of iodine supplementation on a pediatric population with mild iodine deficiency in an ongoing program in the Province of Pontevedra, northwestern Spain. In the first survey (1984), 1565 schoolchildren and in the second survey (1995) 907 schoolchildren were randomly selected from the population. In January 1985, a mandatory consumption of iodized salt in our region was begun. In both surveys we studied prevalence of goiter, urinary iodine excretion, and prevalence of thyroid dysfunction. Similar prevalences of goiter were observed in both surveys, 3.7% versus 3.9%; however, significantly lower prevalence of Ib and II degree goiters were observed in the second survey. The mean iodine excretion was 88.6 +/- 73 microg/L (median 66.3) and 146.4 +/- 99 microg/L (median 115.7), $p < 0.01$ for the first and second surveys, respectively. Finally, the overall prevalence of thyroid dysfunction was similar in both surveys, 9.2% versus 7.0%; however, significantly lower prevalence of suppressed serum thyrotropin (TSH), considered as a marker of subclinical hyperthyroidism, was observed in the second survey when compared to the first, 0.1% versus 2%, $p < 0.01$. Our results are in agreement with the recent data from Denmark, where the prevention of subclinical hyperthyroidism occurring in the elderly as a consequence of longstanding mild iodine deficiency is the reason that the Danish finally started iodine supplementation on a national basis. In conclusion, long-term correction of mild iodine deficiency in a pediatric population has beneficial effects on the prevalence of high-degree goiters, and this correction reduces significantly the prevalence of subclinical hyperthyroidism. The present observation constitutes a strong argument for correcting even mild iodine deficiency. [iodine supplementation reduces rate of hyperT.doc](#)

To evaluate the importance of trace amounts of elements in thyroid cancer etiology and diagnostics, instrumental neutron activation analysis has been used to estimate Ag, Co, Cr, Fe, Hg, I, Rb, Sb, Se, and Zn concentrations in malignant and benign thyroid nodules as well as in apparently intact paranodular thyroid tissue. Resected material from 135 patients was obtained from operations. Forty-five cancer cases were diagnosed and the rest were of benign nodules. The thyroid glands of 65 people, 53 male and 12 female, who died and unexpected death or committed suicide, were used as a control group. Trace element contents of the International Atomic Energy Agency reference material H-4 (animal muscle) were analysed simultaneously with the thyroid tissue in order to evaluate the accuracy of the obtained data. No dependence of trace element contents on sex and age (14-80 years) was found for normal thyroids. In paranodular tissue, the Ag, Co, Hg, I and Rb contents were much higher for malignant and benign nodules than they were for the standard. There was also a slight deficiency of Se in the nodules compared with the standard. This result supports the hypothesis that the direct toxic heavy metal influence on thyrocytes plays a major role in thyroid cancer etiology, provided that an adequate level of the defence mechanisms is absent. Iodine concentrations are 15 times lower, on average, in malignant compared with benign nodules. It is also shown that the ratio between the iodine concentration in nodular and paranodular tissue can be used for in vivo thyroid cancer diagnostics. [iodine low in thyroid cancer, other elements.doc](#)

Geographical distribution patterns of incidence and mortality for a wide variety of diseases display strong positive and negative correlations when analyzed statistically. It is argued that these relationships do not occur by chance, but reflect the causal role of surpluses and/or deficiencies of various bulk and trace elements. This concept is explored for one such "disease family tree", that of iodine. Deficiencies of this essential trace element appear to be associated with many diseases, or birth defects, including goitre, cretinism, multiple sclerosis, amyotrophic lateral sclerosis and cancer of the thyroid and nervous system. Although the evidence is weaker, iodine deficiency may also be implicated in Alzheimer's and Parkinson's diseases. In contrast, too much iodine may be linked to elevated mortality from cancer of the skin and melanoma. Rat studies indicate that iodine deficiencies can cause reduced brain weight, limited myelin formation, retarded neuronal maturation, a lowering of the production of various enzymes and slowing of the rates of protein and R.N.A. synthesis. Similar processes appear to occur in many of the diseases identified above. [iodine--diseases of deficiency and excess.doc](#)

In view of the adverse effects of the administration of pharmacological quantities of iodine to euthyroid patients with a history of a wide variety of thyroid disorders, it has been suggested that iodine-containing medications and radioopaque dyes containing iodine should be avoided, if possible, in patients with underlying thyroid disease. We have now prospectively studied the effects of pharmacological doses of a saturated solution of **potassium** iodide (SSKI) on thyroid function in euthyroid patients with a previous history of hyperthyroid Graves' disease successfully treated with antithyroid drugs. Ten euthyroid women (mean age, 56 yr) who had hyperthyroid Graves' disease successfully treated

with methimazole 36.4 +/- 4.7 months earlier were evaluated before, during, and after the administration of 10 drops SSKI daily for 90 days. The following thyroid function tests were obtained: serum T4, T3, TSH, TSH receptor antibody (TSH-RAb), and antithyroid peroxidase antibody (AbTPO) concentrations; TRH tests; and iodine perchlorate discharge tests. Serum T4, T3, basal and TRH-stimulated TSH, and TSH-RAb values were normal before SSKI administration, but serum AbTPO levels were markedly positive in 7 and iodine perchlorate discharge tests were positive in 4 of these 10 women. During SSKI administration, basal and TRH-stimulated serum TSH values increased above normal in 2 women with normal serum T4 and T3 concentrations; thyroid hormone values and TRH tests were normal in the other 8 patients and similar to values observed in 4 euthyroid women without a history of thyroid disease given SSKI. Serum AbTPO increased slightly, but significantly, during SSKI administration in the 7 women with positive values at baseline ($P < 0.05$). TSH-RAb remained undetectable. After SSKI withdrawal, the 10 women were reevaluated 60 and 120 days later. Two women developed a blunted TSH response to TRH, but normal serum T4 and T3 concentrations, and 2 women developed overt hyperthyroidism, with undetectable basal and TRH-stimulated serum TSH and elevated serum T4 and T3 concentrations, requiring methimazole therapy. All values in the remaining 6 women were similar to those present before SSKI administration. These results suggest that some euthyroid patients with a history of antithyroid drug therapy for Graves' disease may develop thyroid dysfunction during and after excess iodine administration. The development of subclinical hypothyroidism during SSKI administration was not clinically important, but the occurrence of overt hyperthyroidism after SSKI was discontinued did require antithyroid drug therapy. It is advisable, therefore, to avoid iodine-containing substances in euthyroid patients with a history of antithyroid drug therapy for Graves' disease. [iodine effects in pts previously treated with ATD for Graves.doc](#)

To evaluate the importance of trace amounts of elements in thyroid cancer etiology and diagnostics, instrumental neutron activation analysis has been used to estimate Ag, Co, Cr, Fe, Hg, I, Rb, Sb, Sc, Se, and Zn concentrations in malignant and benign thyroid nodules as well as in apparently intact paranodular thyroid tissue. Resected material from 135 patients was obtained from operations. Forty-five cancer cases were diagnosed and the rest were of benign nodules. The thyroid glands of 65 people, 53 male and 12 female, who died and unexpected death or committed suicide, were used as a control group. Trace element contents of the International Atomic Energy Agency reference material H-4 (animal muscle) were analysed simultaneously with the thyroid tissue in order to evaluate the accuracy of the obtained data. No dependence of trace element contents on sex and age (14-80 years) was found for normal thyroids. In paranodular tissue, the Ag, Co, Hg, I and Rb contents were much higher for malignant and benign nodules than they were for the standard. **There was also a slight deficiency of Se in the nodules compared with the standard.** This result supports the hypothesis that the direct toxic heavy metal influence on thyrocytes plays a major role in thyroid cancer etiology, provided that an adequate level of the defence mechanisms is absent. **Iodine concentrations are 15 times lower, on average, in malignant compared with benign nodules.** It is also shown that the ratio between the iodine concentration in nodular and paranodular tissue can be used for in vivo thyroid cancer diagnostics. [cancer of thyroid and trace elements.doc](#)

In genetically predisposed individuals, autoimmune lymphocytic thyroiditis (LT) is potentiated by excess dietary iodine (I). There have been data which suggest that oxidative stress may have a role in iodine-induced LT. These in vivo studies were undertaken to examine the effect of iodine on intrathyroidal levels of the potent antioxidant glutathione (GSH) and see if the thyroids of LT-prone BB/Wor rats have aberrant GSH responses after iodine-loading. LT-prone BB/Wor, non LT-prone BB/Wor and Wistar rats were randomized to receive either 0.05% I (as NaI) or tap water. Thyroid and liver homogenates were assayed individually for GSH. Following the administration of 0.05% iodine water overnight, all of the animals demonstrated a rise in intrathyroidal GSH regardless of LT-proneness. To determine whether this was a dose-dependent response, Wistar rats were randomized to receive tap, 0.0125%, 0.025%, 0.05%, or 0.075% I, overnight. Intrathyroidal GSH levels rose with increasing iodine concentrations peaking at 0.025% I. Hepatic GSH levels were unaltered by iodine treatment. Ten days of 0.05% I water did not result in any difference between the GSH levels of thyroids from treated and control rats. Frozen sections of the thyroids and livers from iodine-treated rats were compared to tap-water controls after staining with Mercury Orange for GSH and Schiff's reagent for evidence of lipid peroxidation. Iodine-treated thyroids had an apparent shift of GSH staining from the apical border to the cytoplasm. However, there was no Schiff's staining indicative of lipid peroxidation in the iodine-treated thyroids. [iodine ingestion increases intrathyroidal glutathione.doc](#)

Iodine-induced thyrotoxicosis or "Jod-Basedow phenomenon" has been reported throughout the world since iodine has been administered to treat endemic goitre. Nowadays, iodinated radiocontrast agents and the antiarrhythmic drug amiodarone are the most common sources of excess iodine load subsequently leading to iodine-induced thyrotoxicosis, especially in elderly patients with underlying goitre. The aim of the study was to identify the number of cases of iodine-induced thyrotoxicosis among patients with thyrotoxicosis in a large urban hospital. Over an 18-month period thyrotoxicosis has been diagnosed in a total of 39 patients. Eight patients with iodine-induced thyrotoxicosis (5 female, 3 male; mean age 60.6 years) have been identified (20%). In all patients with iodine-induced thyrotoxicosis, iodine exposure with a mean iodine dose of 21.5 g was documented 2 to 16 weeks before diagnosis (iodinated radiocontrast agents in 5 patients, amiodarone in 2 patients, kelp tablets in 1 patient). Clinical features were predominantly tachyarrhythmias and heart failure, while 6 of 8 patients had goitre (thyroid volume 31 to 193 ml). Thyroid antibodies were not detected. Diagnosis was confirmed in 5 of 8 patients with increased urinary iodine concentrations (3436 to > 6000 nmol/24 h), and in 3 of 8 patients with a low tracer uptake in thyroid scintigraphy (1 to 4%). Treatment consisted of methimazole in all patients, additional tional beta-blockers and lithium in 4 patients, and prednisone in 5 patients. The mean treatment duration was 9.2 months, and patients became euthyroid after a mean treatment duration of 6.4 weeks. One patient (with still elevated free thyroxine levels) died of myocardial infarction 4 weeks after antithyroid drug therapy had been installed. The incidence, mechanisms and features of iodine-induced thyrotoxicosis are discussed. Iodine-induced thyrotoxicosis is a common disease, and the recognition and treatment of iodine-induced thyrotoxicosis, particularly in elderly patients and patients with goitre, are of clinical importance. [iodine-induced hyperthyroidism.doc](#)

Iodine is a requisite substrate for the synthesis of the thyroid hormones, the minimum daily requirement being about 50 micrograms. An autoregulatory mechanism within the thyroid serves as the first line of defense against fluctuations in the supply of iodine and also permits escape from the inhibition of hormone synthesis that a very large quantity of iodine induces (Wolff-Chaikoff effect and escape therefrom). Environmental iodine deficiency continues to be a significant public health problem worldwide, compounded in some geographic regions by the presence of other goitrogens in some staple foods. The pathologic consequences of severe iodine deficiency include endemic goiter, endemic cretinism, increased fetal and infant mortality, and an increased prevalence in the community of cognitive and neuromotor disabilities. The implementation of an iodization program prevents endemic cretinism and reduces the frequency of the other pathologic consequences of iodine deficiency. Iodine excess results principally from the use of iodine-containing medicinal preparations or radiographic contrast media. The pathologic consequences of iodine excess will ensue only when thyroid autoregulation is defective, in that escape from the Wolff-Chaikoff effect cannot occur, or when autoregulation is absent. Defective autoregulation characterizes the fetal and neonatal thyroid, Hashimoto's thyroiditis, radioiodine or surgically treated Graves' hyperthyroidism, the thyroid of patients with cystic fibrosis, and the thyroid that has been exposed to weak inhibitors of the organic binding of iodine. In these circumstances, the provision of excess iodine may lead to iodide goiter with or without hypothyroidism. Absent autoregulation may be a feature of longstanding multinodular goiter, and the provision of excess iodine in this circumstance may induce thyrotoxicosis (Jod-Basedow disease). The pathologic consequences of iodine excess will resolve when the source of iodine has been dissipated. In addition to its role in reversing iodine deficiency, iodine is used as adjunctive therapy for hyperthyroidism. By inhibiting the proteolytic release of iodothyronines from thyroglobulin, it induces a prompt slowing of thyroid hormone secretion. This effect is exploited in the treatment of thyrotoxic crisis or severe thyrocardiac disease. Iodine also reduces thyroid cellularity and vascularity and therefore is used in the preparation of the patient for thyroidectomy. Finally, by exploiting the failure of escape from the Wolff-Chaikoff effect, iodine may also be used in the early management of radioiodine-treated Graves' hyperthyroidism. [iodine and thyroid disease.doc](#)

In 1990, iodine deficiency affected almost one-third of the world population and was the greatest single cause of preventable brain damage and mental retardation. Following a resolution adopted by the World Summit for Children in 1990, major programmes of iodine supplementation were implemented by the governments of the affected countries with the support of major donors. Iodisation of salt was recognised as the method of choice. Nine years later, by April 1999, 75% of the affected countries had legislation on salt iodisation and 68% of the affected

populations had access to iodised salt. The prevalence of iodine deficiency disorders decreased drastically in most countries and the deficiency disappeared completely in some such as Peru. This result constitutes a public health success unprecedented with a non-infectious disease. However, occasional adverse effects occurred. The principle effect is iodine-induced hyperthyroidism which occurs essentially in older people with autonomous nodular goitres, especially following iodine intake that is too rapid and of too massive an increment. The incidence of the disorder is usually low and reverts spontaneously to the background rate of hyperthyroidism or even below this rate after 1 to 10 years of iodine supplementation. The possible occurrence of iodine-induced thyroiditis in susceptible individuals has not been clearly demonstrated by large epidemiological surveys. Iodine supplementation is followed by an increased prevalence of occult papillary carcinoma of the thyroid discovered at autopsy but the prognosis of thyroid cancer is improved due to a shift towards differentiated forms of thyroid cancer that are diagnosed at earlier stages. Iodine-induced hyperthyroidism and other adverse effects can be almost entirely avoided by adequate and sustained quality control and monitoring of iodine supplementation which should also confirm adequate iodine intake. Available evidence clearly confirms that the benefits of correcting iodine deficiency far outweigh the risks of iodine supplementation.[iodine supplementation--benefits outweigh risks.doc](#)

After a cure with iodine in Bad Hall (Upper Austria), patients with age-related maculopathy repeatedly reported improvement in visual power: the picture seen seems to be clearer on the whole or more distinct. These statements were checked in 50 patients with beginning age-related macula degeneration ('dry form') using the 'Vision Contrast test system (VCTS 6500)'. The analysis of the results showed that there is indeed a statistically highly significant improvement in contrast sensitivity after the cure ($p < 0.0001$). The spontaneous observations of the patients were therefore confirmed by the study. [iodine improves macular degeneration.doc](#)

After taking a cure with iodine treatments in Bad Hall (Upper Austria), patients with eye diseases repeatedly report improvements in their color vision. They state that colors are once again "more saturated, richer, and more distinct." These statements were checked using the Farnsworth Panel D-15 dichotomous test and the Lanthony desaturated 15 Hue test. The analysis of the results showed that there is indeed a statistically significant improvement in color vision after the cure. The spontaneous observations of the patients were therefore confirmed by the study.[iodine improves color vision.doc](#)

Patients must be assessed for iodine allergy prior to indocyanine green administration. A scrupulous injection technique will ensure a safe diagnostic procedure. 2. Indocyanine green dye is used for choroidal angiography to diagnose age-related macular degeneration. 3. Indocyanine green dye has no discernable after effects for the patient. It is nontoxic and wholly removed by the liver. Indocyanine green does not show up as skin discoloration.[iodine dye used for macular degeneration angiography.doc](#)

The effect of in vivo administration of cadmium chloride on the pituitary-thyroidal axis was assessed in 200 g body weight Wistar rats. A dose of 2.5 mg/kg body weight was injected i.v. 24 h before the experiments were initiated. Plasma thyroxine (T4) and tri-iodothyronine (T3) concentrations in cadmium-treated rats were significantly ($P < 0.01$) decreased, whereas plasma TSH failed to increase in response to low T4 and T3. However, the TSH response to TRH and the pituitary content of TSH in these rats were both normal. Cadmium induced a significant ($P < 0.01$) decrease in 4-h thyroidal ^{131}I uptake and in thyroid/plasma radioactivity ratio. The in vitro conversion of T4 to T3 in the pituitary was significantly ($P < 0.01$) blocked by cadmium whereas there was no in vivo effect. Parameters of peripheral T4 kinetics in cadmium-treated rats, such as metabolic clearance rate ($P < 0.01$), fractional turnover rate ($P < 0.01$), absolute disposal rate ($P < 0.05$), urinary clearance ($P < 0.05$) and faecal clearance ($P < 0.05$), were all decreased by cadmium. The lack of response of TSH to low plasma T4 and T3 and the normal response to exogenous TRH in this and in other non-thyroidal illness syndromes produced by other pathologies suggest a decreased stimulation of pituitary thyrotrophs by endogenous TRH.[iodine antagonized by cadmium.doc](#)

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Iodine replacement in fibrocystic disease of the breast.

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OBJECTIVE: To determine the response of patients with fibrocystic breast disease to iodine replacement therapy. **DESIGN:** Review of three clinical studies beginning in 1975: an uncontrolled study with sodium iodide and protein-bound iodide; a prospective, control, crossover study from iodide to molecular iodine; and a prospective, control, double-blind study with molecular iodine. **SETTING:** University affiliated breast-treatment clinics. **PATIENTS:** Study 1: 233 volunteers received sodium iodide for 2 years and 588 received protein-bound iodide for 5 years. Study 2: the treatment of 145 patients from study 1 treated with protein-bound iodide for several months who still had symptoms was switched to molecular iodine 0.08 mg/kg; 108 volunteers were treated initially with molecular iodine. Study 3: 23 patients received molecular iodine, 0.07 to 0.09 mg/kg body weight; 33 received an aqueous mixture of brown vegetable dye and quinine. The numbers in study 2 increased over the review period so that 1365 volunteers were being treated with molecular iodine by 1989. **INTERVENTIONS:** All patients in study 3 had pre- and post-treatment mammography and measurement of serum triiodothyronine, thyroxine and thyroid-stimulating hormone levels. **MAIN OUTCOME MEASURES:** Subjective evaluation--freedom from pain--and objective evaluation--resolution of fibrosis. **RESULTS:** Study 1: 70% of subjects treated with sodium iodide had clinical improvement in their breast disease, but the rate of side effects was high; 40% of patients treated with protein-bound iodide had clinical improvement. Study 2: 74% of patients in the crossover series had clinical improvement, and objective improvement was noted in 72% of those who received molecular iodine initially. Study 3: in the treatment group 65% had subjective and objective improvement; in the control group there was a subjective placebo effect in 33% and an objective deterioration of 3%. **CONCLUSIONS:** The fibrocystic breast reacts differently to sodium iodide, protein-bound iodide and molecular iodine. Molecular iodine is nonthyrotropic and was the most beneficial.

This study basically refers to Thyroiditis, which is an inflammation of the thyroid gland. I have autoimmune hyperthyroidism (Graves'),

but I have been diagnosed as having "chronic thyroiditis" as well.

<http://ehpnet1.niehs.nih.gov/docs/1999/suppl-5/749-752rose/abstract.html>

(Or go to www.nih.gov - and use the "search" feature. Type in "Linking Iodine with Autoimmune Thyroiditis")

From another document I obtained:

"The introduction of dietary iodine as a public health measure in the early twentieth century eliminated endemic goiter in the United States, but may have spawned another set of problems. The incidence of autoimmune thyroiditis is increasing concomitantly with progressively increasing iodine content in the American diet."

"The effects of high iodine uptake, however, are observed only in genetically susceptible individuals."

Carrageenan (sometimes called carrageen moss) is ground up seaweed! It's also used to do marbling, as it's useful property is that it thickens. I should think it's LOADED with iodine.

Interactions between selenium and iodine

April 27, 1999

Selenium and iodine are two minerals which are critically important in the proper functioning of the thyroid. While the importance of iodine has been known a long time, the importance of selenium has only been discovered and explored since 1990. Much research is presently being conducted on the functions of these two minerals in thyroid function and it is becoming clear that there is an interaction between the two. Iodine has a seemingly simple role in the thyroid-it is incorporated into the thyroid hormone molecule.

A deficiency of iodine will cause hypothyroidism and if this is severe and occurs during pregnancy, the offspring will be mentally damaged and is called a cretin. Cretinism, or myxedematous cretinism as it is sometimes called, is not only caused by an iodine deficiency, but is also influenced by a selenium deficiency. Iodine apparently has just one function in the body-in the thyroid.

Selenium, on the other hand, performs many functions. At the beginning of the 1990s it was discovered that the deiodinase enzymes which convert T4 (thyroxin, the thyroid prohormone) into T3 (triiodothyronine, the cellularly active hormone) and also convert T3 into T2, thereby degrading it, are selenium enzymes (formed with the amino acid cysteine). This discovery has led to a lot of research studies on the effects of selenium, iodine, and their interactions.

Selenium also performs other important roles in the body. The most important of these is probably as its role as the body's best antioxidant (anti-peroxidant). It performs this role as part of glutathione peroxidase (GSHPx or GPX). As part of GPX, selenium prevents lipids and fats from being peroxidized (oxidized), which literally means that it prevents fats from going rancid (this can be seen on your skin as "age spots" or "liver spots" (autopsies show that skin "liver spots" are accompanied by similar spots of peroxidized fats in the liver.) Therefore selenium protects all of the cellular membranes, which are made up of fats, from peroxidation. Peroxidation of cellular membranes reduces the ability of the membrane to pass nutrients including minerals and vitamins, so selenium deficiency is the first step toward developing the many problems caused by nutrient deficiencies.

Joel Wallach considers a selenium deficiency combined with high intake of vegetable oils (salad dressings, margarine, cooking oils) as the "quickest route to a heart attack and cancer." It seems that the body uses a lot of selenium to protect the fats from peroxidation. Polyunsaturated fats which are hydrogenated or heated become the same as rancid fats and large amounts of selenium are then needed to protect the body. Consumption of these dietary fats can thus lead to a selenium deficiency.

Selenium is also essential for the production of estrogen sulfotransferase which is the enzyme which breaks down estrogen. A deficiency of selenium can thus lead to excessive amounts of estrogen, which may depress thyroid function, and also upset the progesterone-estrogen balance.

Wallach also lists other effects of selenium deficiency: anemia (red blood cell fragility), fatigue, muscular weakness, myalgia (muscle pain), muscular dystrophy (white muscle disease in animals), cardiomyopathy (sudden death in athletes), heart palpitations, irregular heartbeat, liver cirrhosis, pancreatitis, Lou Gehrig's and Parkinson's diseases (mercury toxicity), Alzheimer's Disease (high intake of vegetable oil), sudden infant death syndrome (and possibly "breathlessness" in adults, jj), cancer, multiple sclerosis, and sickle cell anemia.

Selenium is essential for the production of testosterone. A deficiency seems to be involved in osteoarthritis. I've found studies linking selenium deficiency to alopecia (hair loss) and to degeneration of the knee joint (seen in Kashin-Beck disease). Since selenium is necessary to produce GPX which is a major detoxifier of man-made and environmental toxins, selenium deficiency can lead to chemical and drug sensitivities.

These are some of the non-thyroidal effects of selenium deficiency. The effects of selenium deficiency on thyroidal health is even more interesting. One study I read indicated that in experimental animals, selenium deficiency will increase T3 in the heart. This may be the reason that selenium deficiency causes heart palpitations and rapid heart beat, which is common in thyroid disease.

While we've seen that selenium deficiency will interfere with T4 to T3 conversion and lead to functional hypothyroidism (low T3 phenomenon), selenium plays another vital role in the thyroid as part of GPX. During the production of thyroid hormone, hydrogen peroxide (H2O2) is produced. H2O2 is important for the production of thyroid hormone, but excessive amounts lead to high production of thyroxin (T4) and also damage to the cells of the thyroid. GPX plays the extremely vital role of degrading H2O2 and thereby limiting hormone production and preventing damage to the thyroid cells. This seems to be the main way in which selenium protects the thyroid from sustaining damage which can lead ultimately to cancer.

Without selenium, the thyroid gland becomes damaged and it is through this mechanism that the main selenium and iodine interactions are found. An iodine deficiency will cause goiter, an enlargement of the thyroid gland produced by the body in an attempt to increase hormone production from limited amount of iodine. Selenium deficiency increases the weight of the thyroid in experimental animals, and a selenium deficiency combined with an iodine deficiency leads to a further increase in thyroidal weight (bigger goiter). In African countries like Zaire, there are areas where both iodine and selenium are very scarce in the soil (these deficiencies seem to run parallel in most areas). Consequently a high percentage of the people have goiters and hypothyroidism. An experimental attempt was made to correct the selenium deficiency and the result was that the hypothyroidism was made WORSE in the hypos and it produced hypothyroidism in some euthyroid subjects. This was entirely unexpected and the experimenters issued a warning about supplementing with selenium (and not iodine) when both deficiencies exist concurrently.

The body has a compensatory mechanism to maintain T3 levels when iodine is deficient--it increases the production of the deiodinase Type I enzyme (DI-I). This is not a small increase, but has been shown in cattle to be an increase of 10-12 times. This increase in DI-I increases the conversion of the existing T4 to T3 to maintain T3 levels, but also increases the conversion of T3 to T2 (the degraded by-product of T3). Because of the iodine deficiency, T4 is not replenished and T3 ultimately decreases from the lack of sufficient T4 leading to a worsening of the hypothyroidism.

This result is made worse by another phenomenon which hasn't been thoroughly studied: a selenium deficiency causes an iodine deficiency to get worse. This may be a protective adaptation by the body to limit the damage caused to the thyroid when selenium is deficient and iodine is adequate. Let's examine this part of the interaction.

We've all heard that many doctors tell hypo patients, especially those with Hashimoto's thyroiditis, not to take iodine because it can aggravate their condition. The reason seems to be that selenium protects the thyroid gland from oxidative damage and this damage can increase significantly if iodine is supplemented. Taking iodine will increase thyroid hormone production and the production of H2O2 which damages the thyroidal cells. The lack of selenium prevents GPX from being able to protect the cells from this oxidative damage. While I doubt if most doctors realize why iodine should be restricted (it certainly seemed counter-intuitive to me at first), they have learned through experience that iodine can increase the thyroid damage in Hashimoto's. The information that selenium should be supplemented along with iodine is so new that most of them are unaware of it.

Here's what we have: Studies have shown that if iodine is low, selenium must also be kept low to prevent the hypothyroidism from becoming worse (from increased DI-I and T4 depletion, as explained above.) So if both minerals are low, then the person is hypo and gets a goiter, but the damage to the thyroid is kept to a minimum. More severe problems happen when either selenium or iodine is high and the other is low. If selenium is high and iodine low, then T4 to T3 to T2 conversion is accelerated without T4 being replenished, leading to a worsening of the hypoT. If iodine is high and selenium is low, then H2O2 is not degraded by GPX. Since H2O2 drives the thyroid hormone production, then the thyroid over-produces thyroid hormone (Grave's hyperthyroidism), the thyroid is damaged from the oxidation by the H2O2, and the end result is that the damaged thyroid ultimately decreases activity and hypothyroidism results (Hashimoto's thyroiditis). This could explain the observed progression of Grave's to Hashimoto's.

If a selenium deficiency causes an iodine deficiency, leaving you both selenium and iodine deficient, and supplementing with either selenium or iodine causes severe problems, then the only solution is to supplement both selenium and iodine simultaneously and gradually. Even then you could experience an immediate boost (from increased conversion of T4 to T3) with a subsequent letdown (lack of T4 production because of insufficient iodine or other necessary nutrient). You have to be prepared to ride out the tough times and continue increasing the selenium and iodine until those two deficiencies are corrected and the respective metabolic pathways are back working properly.

Everything that I've read about selenium indicates that it is absolutely essential for proper functioning of the thyroid. A deficiency of selenium may lead to either hyperthyroidism or hypothyroidism. I've always wondered if high intake of selenium can lead to hyperthyroidism and finally found someone who did the experiment. They found that a high intake of selenium will not increase T4 production and lead to hyperthyroidism.

If a person has hyperT, then it looks like taking selenium without iodine will result in a decrease in production of T4 (although there may be an initial transient increase in T4 to T3 conversion and hence higher T3). I would suggest to start with a small amount of selenium methionine (about 50 mcg) and gradually increase it. I cannot see any way that thyroid function can be normalized without selenium.

For hypos the important message is that a selenium deficiency may cause an iodine deficiency, so that even though you are taking iodine you may not be assimilating it unless selenium is also being taken. This would explain how people can have iodine deficiencies even though salt and many foods have iodine added. Supplement with both iodine and selenium. I would recommend starting with 100 mcg of selenium and one kelp tablet and gradually work up to 400-600 mcg of selenium and 2-4 tablets of kelp.

While I've found research on the interactions of iodine and selenium, there are two other minerals which need to be studied for their interactions with these two: zinc and copper. I found one study which examined the complex interactions of selenium, iodine, and zinc (there are interactions), but none which have looked at all four minerals in a 4 X 4 factorial design. Now that would be an interesting study! Hopefully someone will do that soon.

I think one lesson from studying the interactions of selenium and iodine is that the interrelationships between minerals are very complicated. Supplementing with one or two can cause further problems. You have to make sure that you correct every deficiency. Health is built from a chain of nutrients and, like a chain, health cannot be accomplished if one nutrient is missing. Sometimes it's complicated putting the chain back together without running into problems (like supplementing with either selenium or iodine, but not both), but every deficiency has to be corrected. John

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Anti-goitrous effect of lecithin-bound iodine in propylthiouracil treated rats.

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OBJECTIVE: Excess iodine and some iodine-containing compounds are known to affect various parameters of thyroid function. Lecithin-bound iodine (LBI) is a compound which induces involution of an enlarged thyroid. LBI was tested for its ability to affect thyroid ornithine decarboxylase (ODC) activity and apoptosis. **METHODS:** LBI was given orally to propylthiouracil-pretreated rats and the changes in ODC activity and apoptosis were observed. The thyroid apoptosis was detected by DNA laddering and flow cytometry.

RESULTS: LBI suppressed the thyroid ODC activity within one hour after its administration and lowered slightly but significantly the thyroid putrescine levels at 3 h. The DNA cleavage ladder was evident at 3-6 h after LBI treatment. Propylthiouracil induced thyroid enlargement was reduced significantly at 3 days after chronic treatment with LBI. The thyroidal content of putrescine was also decreased after chronic treatment. These effects of LBI were essentially the same as those of excess iodide, while other iodinated compounds including amiodarone, iopanoic acid and erythrosine had no effect on the thyroid ODC activity.

CONCLUSIONS: These results suggest that LBI may exert its anti-goitrous effects, consisting of the inhibition of ODC activity and apoptosis, in the form of inorganic iodide in vivo.

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Iron is a very critical mineral for persons with thyroid disease. There is a high association between hyperthyroidism and anemia and while most of those cases of anemia are from copper deficiency, it is possible that some of them are from iron deficiency.

Many hypos also seem anemic and it's possible that in hypothyroidism, anemia stems more often from iron deficiency than from copper deficiency.

The balance of the three minerals, copper, zinc, and iron, is critically important in preventing and correcting thyroid diseases. Each of these three minerals antagonizes and can deplete the other two. Many times the antagonistic and depletion effects are not due to competition in absorption, but because these minerals work together.

We can think of these three minerals as corners of a triangle. Each one affects the other two. If any one of the three is ingested in large amounts it depletes the other two. Likewise if one of the three gets deficient, then the other two may not be utilized and therefore build up in the liver, hair, or other tissues.

For example, if zinc gets too high in the body, copper and iron will get depleted with the result of anemia and (probably) hyperthyroidism. If two of the three minerals are high, then the third mineral will get very depleted. For example, high intake of both iron and copper could deplete zinc and cause hypothyroidism.

An interesting pair to look at is copper and iron. Copper and iron work together to form hemoglobin, the oxygen-carrying molecule in the red blood cell. The two minerals have to be present in a balanced amount, usually about 5:1, and if one of the two is supplied in higher amounts it can cause the other to be depleted.

We see this when people take large amounts of iron to correct anemia. Anemia can be caused by iron deficiency or copper deficiency (or B-12 or other vitamin deficiencies), but most people and doctors assume that anemia is always caused by iron deficiency.

Taking large amounts of iron when it is copper that is deficient will cause copper to be further depleted and lead to a worsening of the anemia. I believe this is one practice that can lead to hyperthyroidism. It's possible that the addition of nutritional supplements like iron to foods may also contribute to thyroid disease. For example, iron is added to many food products, especially breakfast cereals, breads, and other grain products. We know that excess iron will deplete copper, so it's possible that eating iron fortified foods is a contributing factor to hyperthyroidism.

IRON

If one of the pair gets deficient then the other will not be able to be used effectively and will build up in the liver or other tissues. For example, if iron gets deficient, then copper may build up in the liver, hair, and appear as rings or spots in the iris of the eyes. These accumulations of copper occur in Wilson's Disease, a disease which is described as a hereditary disease of copper buildup. Whether Wilson's disease is caused by iron or zinc deficiencies is unknown but many Wilson's patients take zinc to keep copper levels low (often along with a copper chelator).

There is one subset of hyperthyroids who have high copper levels in the hair and presumably also have high copper accumulations in the liver. These people often manifest schizophrenic or manic-depressive symptoms. In fact one of the characteristics of these psychiatric symptoms is high copper levels which can be detected in the hair. Also these conditions are highly associated with hyperthyroidism.

One of the hypotheses that I'm working on is that this subset of hyperthyroidism, where the person has high copper levels, may be caused by iron deficiency, with a "functional" copper deficiency caused because the lack of iron is preventing the copper that is present from being effectively used. I don't think zinc is deficient in these people because if that were true, the person would probably be hypothyroid.

What happens when copper and zinc are high and iron gets depleted? I can tell you from personal experience that bad things happen. I just went through this through a serious oversight on my part and my failure to supplement iron along with copper and zinc. I'd like to relate the story so that others don't have to go through the same problems. Here's what happened:

At Christmas time I got the flu and it was quite severe. To mitigate the symptoms and hopefully get over it, I did what I tell people not to do: I stopped taking iron, because viruses and bacteria need iron to live, just as we do. This is an effective but unwise strategy for stopping a cold or flu. Many people do this inadvertently when they stop eating red meat and then go for years without getting sick. They think they have become very healthy because they are no longer getting sick, but what they've actually done is make their body so depleted in iron and copper that even viruses can't live there. They usually go along happily until they get hyperthyroidism. I've done this very thing.

When I stopped taking iron, I started developing pains in my abdomen that concentrated on the left side (left side pain that some people have reported?). The pains migrated around my left side, sometimes higher, sometimes lower, sometimes in the front and sometimes in the back. They seemed to be pains in the liver, pancreas, and kidneys. In addition, I had pains in the ribs, mostly in the left side but sometimes in the right

side, which seemed to be caused by calcium deficiency, but yet calcium or magnesium didn't correct the problem. On top of all this I couldn't sleep well and started getting nighttime rapid heart beat.

These pains got worse and worse over the following months and on the occasions when I did try iron, I had negative symptoms immediately afterward. However, after I started looking at iron, I discovered that the following day is when I got the benefits, while at the time I was concentrating on the immediate negative effects.

I tried just about every combination of vitamins and minerals except taking iron but could not figure out what was wrong. I fasted, went on raw foods, and tried a vegetable only diet. Nothing helped. Also I noticed that every high copper food was making it worse. Nuts, beans, chocolate, and beer increased the symptoms so I discontinued them.

I finally got a critical clue when I went to the mountains snowboarding. I got out of breath frequently and it reminded me of years ago when I was anemic. In fact I was anemic. Then I started getting dizzy and feeling I might faint. The clues were hitting me in the head, but for some reason I was not paying attention. I think it's because I'm male and males are not supposed to need iron like females. What I didn't take into consideration was that I was supplementing copper, about 5 mgs. per day.

A couple days after returning from the mountains, I had a dream that all my relatives were coming to visit me because I was dying. As you can imagine that is a disturbing dream! That morning I got up and the inspiration came to me to take iron. Within one hour of taking 25 mgs. I started feeling better, so I took another 25 mgs. I continued to improve so I took another 50 mgs.

By that night 50% of my symptoms were gone. I slept through the whole night without waking once, which hadn't happened in many months. After another day of taking 100 mgs. of iron, 75% of my symptoms were gone and I again slept the whole night without waking. I was back to life.

This was a good lesson for me. I recalled that through the last 20 years whenever I have serious, chronic health problems they always turn out to be mineral deficiencies. I always think I have some vitamin deficiency or feel like I'm being poisoned.

I would try all different kinds of vitamins, fast, eat raw foods, eat only vegetables, eat only potatoes, etc. trying to find the answer. Then after months of getting worse despite all my efforts I would discover it's a mineral deficiency. I would take the mineral, feel much better in only a few hours, and then recover completely over the next couple weeks. It's taken me a very long time to learn this lesson.

Minerals are the key to health and just about every disease is the result of mineral deficiencies. When you take the right mineral, you might feel better in hours or you might feel worse immediately. However, usually within the next day or two you feel significantly better. It always amazes me how fast health returns once the right nutrient is supplied to the body. When we have a mineral deficiency we deteriorate slowly, but when it is corrected, we improve very fast. Underneath our sickness is a body crying for nutrients!

ABSORBING IRON

Getting enough iron is difficult for many people. This is probably why iron deficiency is still the number one nutritional deficiency world-wide.

Iron absorption from foods is very limited. The Nutrition Almanac states that only 2 to 10% of the iron in beans, fruits, and vegetables is absorbed. Animal sources of iron are better absorbed. While the body can use several forms of iron, such as ferric or ferrous iron (ferrous is better), the best form is heme iron. Actually heme iron makes other forms of iron more absorbable, so it's probably best to take an iron supplement with a meal of red meat.

Some things can interfere with iron absorption. Lack of hydrochloric acid in the stomach is a big reason. Person on a low salt diet might not be getting enough chlorine (the Cl in NaCl) and therefore not able to produce enough HCl. Taking a good digestive enzyme with the iron supplement should assist the absorption.

Too high an alkaline diet might interfere since iron needs an acid environment. Eat more acid foods with your iron. Too much roughage in the diet can speed up intestinal transit time and reduce iron absorption. Too much coffee, tea, phytates (from grains), oxalates (spinach, rhubarb), and phosphates can all interfere with iron absorption.

There are nutrients which need to be present for iron absorption: B-12 (try a high potency, 3000 mcg); folic acid (400-800 mcg); vitamin C (1000 mgs); vitamin A; copper; calcium; manganese; molybdenum; and other of the B complex vitamins.

Excessive intake of vitamin E and zinc can interfere with iron absorption. Vitamin E in amounts like 800-1000 IU per day can cause iron deficiency (causing ear aches). Don't take more zinc than iron, since that can also deplete iron.

If all else fails, you might want to experiment with different levels of the B vitamins. It may be that you need more B vitamins and need to get up the the 200 mgs per day quantity. However, I'd try the other things first.

IRON STUDIES

Hemochromatosis is a disease of iron accumulation with resultant damage to the liver, pancreas, heart, and pituitary. Premenopausal women are protected from getting it because of menstrual blood loss. While many people believe it is a hereditary disease, I believe it is a disease of copper deficiency. When copper gets deficient, the body can't use iron so it accumulates and causes damage. The disease is also called siderosis, which is characterized by a gray pallor to the skin from iron accumulation in the tissue.

The first study concludes "The frequency of thyroid disorders in men with hemochromatosis is about 80 times that of men in the general population." What this means is that when men get copper deficient, they get iron accumulation and thyroid disorders.

I've also seen information that links hemochromatosis to a deficiency of selenium and copper.

Title

Thyroid disease in hemochromatosis. Increased incidence in homozygous men.

Author

Edwards CQ; Kelly TM; Ellwein G; Kushner JP

Source

Arch Intern Med, 143(10):1890-3 1983 Oct

Abstract

The thyroid function of 49 patients homozygous for the hemochromatosis allele was studied by measurement of serum thyroxine and thyrotropin concentrations. Of 34 homozygous men, three were found to be hypothyroid (thyroxine, less than 3.0 micrograms/dL and thyrotropin, greater than 40 IU/mL) and one was hyperthyroid (thyroxine, 24 micrograms/dL). All 15 homozygous women had normal thyroid function. The hypothyroid patients had elevated titers of antithyroid antibodies. Histologic examination of the thyroid at autopsy of one hypothyroid patient showed notable *iron* accumulation and fibrosis with modest lymphocytic infiltration. The causative importance of *iron* deposition in thyroid diseases associated with hemochromatosis was suggested by the reversal of the usual sex ratio of thyroid dysfunction. Men with hemochromatosis had a much greater *iron* load than women, and they also had a surprisingly higher incidence of thyroid disease. *Iron* may have caused injury to the thyroid, followed by the development of antithyroid antibodies and hypothyroidism. **The frequency of thyroid disorders in men with hemochromatosis is about 80 times that of men in the general population.**

The following study indicates that iron helps to reduce goiter size. This is excellent evidence that iron is critical for thyroid function and that iron-deficiency anemia is often an important factor in causing hypothyroidism.

Eur J Endocrinol 2000 Mar;142(3):217-223

Iron supplementation in goitrous, iron-deficient children improves their response to oral iodized oil.

Zimmermann M, Adou P, Torresani T, Zeder C, Hurrell R.

Human Nutrition Laboratory, Swiss Federal Institute of Technology (ETH), Zurich, Switzerland.
michael.zimmermann@ilw.agrl.ethz.ch

OBJECTIVE: In developing countries, many children are at high risk for both goiter and iron-deficiency anemia. Because iron deficiency may impair thyroid metabolism, the aim of this study was to determine if iron supplementation improves the response to oral iodine in goitrous, iron-deficient anemic children. **DESIGN:** A trial of oral iodized oil followed by oral iron supplementation in an area of endemic goiter in the western Ivory Coast. **METHODS:** Goitrous, iodine-deficient children (aged 6-12 years; n=109) were divided into two groups: Group 1 consisted of goitrous children who were not anemic; Group 2 consisted of goitrous children who were iron-deficient anemic. Both groups were given 200mg oral iodine as iodized oil. Thyroid gland volume using ultrasound, urinary iodine concentration (UI), serum thyroxine (T(4)) and whole blood TSH were measured at baseline, and at 1, 5, 10, 15 and 30 weeks post intervention. Beginning at 30 weeks, the anemic group was given 60mg oral iron as ferrous sulfate four times/week for 12 weeks. At 50 and 65 weeks after oral iodine (8 and 23 weeks after completing iron supplementation), UI, TSH, T(4) and thyroid volume were remeasured. **RESULTS:** The prevalence of goiter at 30 weeks after oral iodine in Groups 1 and 2 was 12% and 64% respectively. Mean percent change in thyroid volume compared with baseline at 30 weeks in Groups 1 and 2 was -45.1% and -21.8% respectively (P<0.001 between groups). After iron supplementation in Group 2, there was a further decrease in mean thyroid volume from baseline in the anemic children (-34.8% and -38.4% at 50 and 65 weeks) and goiter prevalence fell to 31% and 20% at 50 and 65 weeks. **CONCLUSION:** Iron supplementation may improve the efficacy of oral iodized oil in goitrous children with iron-deficiency anemia.

Title

The effect of iron supplementation on GSH levels, GSH-Px, and SOD activities of erythrocytes in L-thyroxine administration.

Author

Seymen O; Seven A; Candan G; Yigit G; Hatemi S; Hatemi H

Address

Department of Physiology, Cerrahpasa Medical Faculty, Istanbul University, Turkey.

Source

Acta Med Okayama, 51(3):129-33 1997 Jun

Abstract

Our aim was to study the effect of iron supplementation on the following aspects of erythrocyte metabolism in experimental hyperthyroidism: *glutathione* (GSH) levels, *glutathione* peroxidase (GSH-Px), and superoxide dismutase (SOD) activities. Hyperthyroidism induced by L-thyroxine administrations significantly raised erythrocyte GSH, GSH-Px and SOD levels of the rats (P < 0.001). Likewise, we observed that iron supplementation induced significant rises in erythrocyte GSH, GSH-Px and SOD levels (P < 0.001) as compared with the control group. The erythrocyte GSH, GSH-Px and SOD levels of hyperthyroidism-induced iron-supplemented animals were significantly higher when compared with either the iron-supplemented group (P < 0.001) or the only L-thyroxine-administered hyperthyroid group (P < 0.001, P < 0.05, P < 0.01, respectively). The results of this study show that L-thyroxine administration and/or iron supplementation increases GSH, GSH-Px and SOD levels of erythrocytes.

[Changes in brain monoamine neurotransmitter in iron deficiency nonanemic rats].

[Article in Chinese]

Hu R, Wei M, Ding X

Department of Pediatrics Affiliated Hospital, Shandong Medical University, Jinan.

An iron deficiency nonanemic rat model was established by feeding with low-iron diet (11.9 mg/kg) to study if there exists biochemical abnormality in brain tissues. Iron contents of the brain, activities of monoamine oxidase (MAO) in the corpus striatum, and the contents of monoamine neurotransmitter and its metabolite in the cerebral cortex and hippocampus were determined by DCP-AES technique, enzyme histochemical method, and high performance liquid chromatography with electrochemical detection (HPLC-ECD), respectively. Results showed that iron contents and activities of MAO in brain tissues of iron deficiency nonanemic rats reduced significantly, and contents of norepinephrine (NE) and 5-hydroxytryptamine (5-HT) in cerebral cortex were significantly higher than those of controls, while 5-hydroxytryptamine acid (5-HIAA) metabolite of 5-HT in the hippocampus was lower than that of controls. It indicated that there existed metabolic abnormality of monoamine neurotransmitter in the brain tissues of iron deficiency nonanemic rats. Also, this study laid a biochemical basis for abnormal mental and behavioral development caused by iron deficiency.

PMID: 9388911, UI: 98050294

Crit Rev Food Sci Nutr 1999 Mar;39(2):131-48

Iron, thermoregulation, and metabolic rate.

Rosenzweig PH, Volpe SL

University of Massachusetts, Department of Nutrition, Chenoweth Lab, Amherst 01003-1420, USA.

Iron plays an important role, not only in oxygen delivery to the tissues, but also as a cofactor with several enzymes involved in energy metabolism and thermoregulation. As a result, much research has been dedicated to understanding the ramifications of iron depletion and iron deficiency anemia on the physiological functions of these enzymes. There is evidence to suggest that iron depletion and iron deficiency anemia cause physiological changes in the body not only during exercise, but also under resting conditions. Both rat and human studies have produced results revealing elevated levels of norepinephrine in the blood and urine of iron-deficient anemic subjects. These studies also provide evidence to suggest that elevation in metabolic rate may ultimately lead to slower growth rates and lower body weights in iron-deficient anemic animals and humans. The focus of this review is on the effects of iron deficiency on metabolic rate and thermoregulation. Prior to this discussion, a brief background on iron is presented.

PMID: 10198751, UI: 99214964

Redox Rep 1999;4(5):243-50

Derangement of Kupffer cell functioning and hepatotoxicity in hyperthyroid rats subjected to acute iron overload.

Boisier X, Schon M, Sepulveda A, Basualdo A, Cornejo P, Bosco C, Carrion Y, Galleano M, Tapia G, Puntarulo S, Fernandez V, Videla LA

Programas de Farmacologia Molecular y Clinica, Facultad de Medicina, Universidad de Chile, Santiago.

[Medline record in process]

Liver oxidative stress, Kupffer cell functioning, and cell injury were studied in control rats and in animals subjected to L-3,3',5-tri-iodothyronine (T3) and/or acute iron overload. Thyroid calorigenesis with increased rates of hepatic O₂ uptake was not altered by iron treatment, whereas iron enhanced serum and liver iron levels independently of T3. Liver thiobarbituric acid reactants formation increased by 5.8-, 5.7-, or 11.0-fold by T3, iron, or their combined treatment, respectively. Iron enhanced the content of protein carbonyls independently of T3 administration, whereas glutathione levels decreased in T3- and iron-treated rats (54%) and in T3Fe-treated animals (71%). Colloidal carbon infusion into perfused livers elicited a 109% and 68% increase in O₂ uptake in T3 and iron-treated rats over controls. This parameter was decreased (78%) by the joint T3Fe administration and abolished by gadolinium chloride (GdCl₃) pretreatment in all experimental groups. Hyperthyroidism and iron overload did not modify the sinusoidal efflux of lactate dehydrogenase, whereas T3Fe-treated rats exhibited a 35-fold increase over control values, with a 54% reduction by GdCl₃ pretreatment. Histological studies showed a slight increase in the number or size of Kupffer cells in hyperthyroid rats or in iron overloaded animals, respectively. Kupffer cell hypertrophy and hyperplasia with presence of inflammatory cells and increased hepatic myeloperoxidase activity were found in T3Fe-treated rats. It is concluded that hyperthyroidism increases the susceptibility of the liver to the toxic effects of iron, which seems to be related to the development of a severe oxidative stress status in the tissue, thus contributing to the concomitant liver injury and impairment of Kupffer cell phagocytosis and particle-induced respiratory burst activity.

PMID: 10731099, UI: 20193365

: J Basic Clin Physiol Pharmacol 1999;10(4):315-25

Evaluation of antioxidant status in liver tissues: effect of iron supplementation in experimental hyperthyroidism.

Seymen HO, Seven A, Civelek S, Yigit G, Hatemi H, Burcak G

Department of Physiology, Cerrahpasa Medical Faculty, Istanbul University, Turkey. seymano@yahoo.com

The antioxidant defense system in liver tissue in experimental hyperthyroidism and/or in iron supplementation was investigated. Thyroid hormones (T3, T4, TSH), ferritin (marker of iron status), antioxidant status components (glutathione [GSH], glutathione peroxidase [GSH-Px], superoxide dismutase [SOD]), and serum transaminases (GOT and GPT, both of which are known to be released

from damaged hepatocytes), were measured. Hyperthyroidism in rats, induced by L-thyroxine administration, significantly raised SOD activity ($p < 0.05$), but significantly decreased GSH-Px activity and GSH values ($p < 0.001$) in the liver. In the L-thyroxine administered and iron supplemented (TI) group, GSH and GSH-Px values of liver tissues were significantly lower than those of control rats ($p < 0.05$). GSH-Px levels of the TI group were higher ($p < 0.001$), and SOD levels significantly lower ($p < 0.001$) than those of the L-thyroxine administered group. We conclude that hyperthyroidism induces SOD activity in liver; ferritin levels increase in hyperthyroidism, contributing to the antioxidant defense system; GSH-Px and GSH levels are decreased significantly in hyperthyroidism either due to inactivation due to increased oxidative stress or to insufficient synthesis; iron supple- and GPT analysis); iron decreases the effect of T4. This must be taken into consideration during iron supplementation.

PMID: 10631595, UI: 20097170

: *South Med J* 1997 Jun;90(6):637-9

Ferrous sulfate-induced increase in requirement for thyroxine in a patient with primary hypothyroidism.

Shakir KM, Chute JP, Aprill BS, Lazarus AA

Department of Internal Medicine, National Naval Medical Center, Bethesda, MD 20889-5600, USA.

Recent studies have shown that under experimental conditions ferrous sulfate may reduce the gastrointestinal absorption of orally administered levothyroxine sodium in patients with primary hypothyroidism. We describe a patient who became hypothyroid while taking ferrous sulfate. The hypothyroid status was corrected by increasing the dose of levothyroxine. Subsequently, when ferrous sulfate was discontinued, the patient became hyperthyroid while taking the higher dose of thyroid hormone preparation. Since both hypothyroidism and iron deficiency anemia may coexist, additional thyroid function testing is recommended in patients treated concurrently with ferrous sulfate and L-thyroxine.

PMID: 9191742, UI: 97335076

: *J Biol Chem* 1996 May 17;271(20):12017-23

Thyroid hormone modulates the interaction between iron regulatory proteins and the ferritin mRNA iron-responsive element.

Leedman PJ, Stein AR, Chin WW, Rogers JT

Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts 02115, USA.

The cytoplasmic iron regulatory protein (IRP) modulates iron homeostasis by binding to iron-responsive elements (IREs) in the transferrin receptor and ferritin mRNAs to coordinately regulate transferrin receptor mRNA stability and ferritin mRNA translational efficiency, respectively. These studies demonstrate that thyroid hormone (T3) can modulate the binding activity of the IRP to an IRE in vitro and in vivo. T3 augmented an iron-induced reduction in IRP binding activity to a ferritin IRE in RNA electrophoretic mobility shift assays using cytoplasmic extracts from human liver hepatoma (HepG2) cells. Hepatic IRP binding to the ferritin IRE also diminished after in vivo administration of T3 with iron to rats. In transient transfection studies using HepG2 cells and a human ferritin IRE-chloramphenicol acetyltransferase (H-IRE-CAT) construct, T3 augmented an iron-induced increase in CAT activity by approximately 45%. RNase protection analysis showed that this increase in CAT activity was not due to a change in the steady state level of CAT mRNA. Nuclear T3-receptors may be necessary for this T3-induced response, because the effect could not be reproduced by the addition of T3 directly to cytoplasmic extracts and was absent in CV-1 cells which lack T3-receptors. We conclude that T3 can functionally regulate the IRE binding activity of the IRP. These observations provide evidence of a novel mechanism for T3 to up-regulate hepatic ferritin expression, which may in part contribute to the **elevated serum ferritin levels seen in hyperthyroidism**.

PMID: 8662626, UI: 96216126

The following study describes a 62-year old male with sideroblastic anemia, which is anemia with excessive iron deposition in the liver and other cells of the body, and hyperthyroidism. My analysis of this is that the man had a copper deficiency which created the iron build-up and the hyperthyroidism.

Medicina (B Aires) 1995;55(6):693-6

[Acquired sideroblastic anemia and cholestasis in a hyperthyroid patient treated with methimazole and atenolol].

[Article in Spanish]

Mamianetti A, Munoz A, Ronchetti RD, Maccione E, Poggi U, Mugnolo R, Gallo O

Departamento de Medicina Interna, Hospital Aeronautico Central, Buenos Aires, Argentina.

The authors describe a 62 year-old white male who was diagnosed as autoimmune hyperthyroidism and treated with methimazole and atenolol. Ten days later he showed itching, jaundice and choluria. All drugs were discontinued. The patient was given radioactive iodine. Two months later direct serum bilirubin levels reached 35 mg%. Endoscopic retrograde cholangiogram evidenced normal extrahepatic biliary ducts. The percutaneous liver biopsy showed marked cholestasis specially in the centrilobular zone with a slight infiltrate of mononuclear cells in the portal areas. Together with the liver disease the patient presented an anemic syndrome. Bone marrow aspiration showed rich cellularity, Perls staining showed 70% sideroblasts, with 10% ringed sideroblasts and increased extracorporeal iron. The patient's evolution was satisfactory. Twenty months after the beginning of the disease clinical and biochemical tests were normal. A new bone marrow aspiration rendered normal. Hepatic cholestasis suffered by our patient was probably due to an adverse reaction of methimazole. Physiopathology of reversible sideroblastic anemia is discussed.

PMID: 8731582, UI: 96340505

Ferritin is a combination of iron and apoferritin, which is an iron-transporting protein. In the following study it is noted that serum ferritin levels increase in hyperthyroidism, meaning that there is excess iron. In fact, the serum ferritin levels of four anemic patients were significantly higher than those of nine nonanemic

patients. (I'll bet the researchers couldn't figure that one out!)

I believe that ferritin levels are high because of a copper deficiency and that once the thyroid hormone levels are decreased (through antithyroid medication), copper is not being used up to de-activate the hormones, and copper levels increase. This decreases the ferritin level and increases hemoglobin (because the iron now has copper to combine with to form hemoglobin).

Clin Investig 1993 Dec;72(1):26-9

Evaluation of increased serum ferritin levels in patients with hyperthyroidism.

Kubota K, Tamura J, Kurabayashi H, Shirakura T, Kobayashi I

Department of Medicine, Kusatsu Branch Hospital, Gunma, Japan.

To further elucidate the mechanism of increased serum ferritin levels in hyperthyroidism, the changes in erythrocytes and serum iron and total iron-binding capacity levels were examined in addition to serum ferritin levels in 13 hyperthyroid patients. **The mean values of hemoglobin, red blood cells, and packed cell volume were increased by antithyroid therapy.** While the serum levels of iron did not change, those of total iron-binding capacity increased significantly after achieving a euthyroid state. **Increased serum ferritin levels returned to normal through antithyroid therapy. Furthermore, the serum ferritin levels of four anemic patients were significantly higher than those of nine nonanemic patients.** Thus it is concluded that the increase in serum ferritin levels in patients with hyperthyroidism may be due to the direct action of thyroid hormones on its synthesis, while in some cases complicated with anemia impaired iron utilization by erythropoietic cells may also be involved.

PMID: 8136612, UI: 94184112

The following study shows that liver ferritin synthesis is not elevated in hypothyroidism as it is in hyperthyroidism. This indicates that copper is not made deficient by experimental hypothyroidism induced by PTU.

: *Thyroidology* 1992 Dec;4(3):93-7

Relation between thyroid status and ferritin metabolism in rats.

Deshpande UR, Nadkarni GD

Radiation Medicine Centre, B.A.R.C., Bombay, India.

Rats were made hypo and 'hyperthyroid' with propylthiouracil (PTU) and L-Thyroxine (L-T) respectively. The hypo and hyperthyroid status in these rats were confirmed by serum level of T4 and T3. **Liver iron was significantly increased in both the hypo and hyperthyroid animals. However, liver ferritin synthesis rate was reduced by 36% in hypothyroid rats, and elevated by 38% in hyperthyroid ones.** A similar trend was seen in liver ferritin concentration. Further, serum transaminases were elevated only in animals of the hyperthyroid group. It appears from the present data that ferritin metabolism is influenced by thyroid hormone as well as by iron. Thus, the raised serum ferritin in hyperthyroid patients may be partially attributed to increased ferritin synthesis in the liver and its possible leakage into circulation.

Iron is used for staining tissue for the demonstration of glycosaminoglycan (GAG) deposition in the skin, which is seen in pretibial myxedema of Graves' Disease. I'm not sure exactly what this means at this point but hope to fit this in at some time.

J Histochem Cytochem 1984 Oct;32(10):1121-4

Histochemical evaluation of glycosaminoglycan deposition in the skin.

Kupchella CE, Matsuoka LY, Bryan B, Wortsman J, Dietrich JG

Histologic demonstration of glycosaminoglycan (GAG) deposition in the skin has been based on the use of either colloidal iron or alcian blue. To define the best technique for the determination of skin GAG content we undertook a prospective study comparing the two stains and evaluating the use of cetylpyridinium chloride (CPC) to enhance fixation. Slides were prepared from skin biopsies obtained from five patients with cutaneous mucinosis. The preparations were coded and examined by three observers. Colloidal iron staining gave a higher intensity for GAG deposits in papillary and reticular dermis. Digestion by specific enzymes identified similar GAGs with either colloidal iron, or alcian blue; however, colloidal iron made GAGs more obvious, partly due to the contrast afforded by the yellow background stain. The addition of CPC to the fixative appreciably enhanced GAG fixation without interfering with the action of enzymes. Experimentally, we confirmed this effect of CPC by determining a pronounced decrease in GAG leakage into the fixative from CPC treated human umbilical cord. We conclude that the combination of CPC fixation and colloidal iron staining gives the best definition of skin GAGs in clinical specimens.

The following study concludes "that during thyrotoxicosis the supply of iron into erythroblasts is greater than the amount used for haemoglobin synthesis." Since hemoglobin production also requires copper, this is indicative of a copper deficiency in hyperthyroidism.

Scand J Haematol 1980 Sep;25(3):237-43

Sideroblasts and haemosiderin in thyrotoxicosis.

Lahtinen R

Bone marrow sideroblasts and haemosiderin were studied in 19 thyrotoxic patients before therapy and in the euthyroid state. The proportion of sideroblasts and the amount of haemosiderin were significantly higher in the hyperthyroid than in the euthyroid phase. Pathological sideroblasts with coarse perinuclear iron granules were found before therapy but not in the euthyroid phase. **It is concluded that during thyrotoxicosis the supply of iron into erythroblasts is greater than the amount used for haemoglobin**

synthesis.

Because aluminum interferes with iron metabolism, studies have found that people who eat food cooked in aluminum pots get anemia. Getting these people to switch to iron cookware greatly reduces the rate of anemia.

Lancet 1999 Feb 27;353(9154):712-6

Effect of consumption of food cooked in iron pots on iron status and growth of young children: a randomised trial.

Adish AA, Esrey SA, Gyorkos TW, Jean-Baptiste J, Rojhani A

School of Dietetics and Human Nutrition, McGill University, St Anne-de-Bellevue, Quebec, Canada.

BACKGROUND: In less-developed countries, novel strategies are needed to control iron-deficiency anaemia, the most common form of malnutrition. METHODS: We undertook a community-based randomised controlled trial to assess the effects of iron or aluminium cooking pots in young Ethiopian children. Analysis was by intention-to-treat. The primary outcomes were change in children's haemoglobin concentration, weight, or length over the study period. We also did a laboratory study of total and available iron in traditional Ethiopian foods cooked in iron, aluminium, and clay pots. FINDINGS: 407 children, one per household, entered the study. The change in haemoglobin concentration was greater in the iron-pot group than in the aluminium-pot group (mean change to 12 months 1.7 [SD 1.5] vs 0.4 [1.0] g/dL; mean difference between groups 1.3 g/dL [95% CI 1.1-1.6]). The mean differences between the groups in weight and length gain to 12 months (adjusted for baseline weight or length) were 0.6 cm (95% CI 0.1-1.0) and 0.1 kg (-0.1 to 0.3). The laboratory study showed that total and available iron was greatest in foods cooked in iron pots, except for available iron in legumes for which there was no difference between types of pot. INTERPRETATION: Ethiopian children fed food from iron pots had lower rates of anaemia and better growth than children whose food was cooked in aluminium pots. Provision of iron cooking pots for households in less-developed countries may be a useful method to prevent iron-deficiency anaemia.

Iron deficiency may be a factor in anemia, hypothyroidism, and myxedema (pretibial myxedema is a swelling of the front of the shin from fibroblast proliferation, a condition associated with thyroid disease and thyroid eye disease). There are not many studies which have looked at iron levels in myxedema, but the following study is suggestive.

Lik Sprava 1999 Jun;(4):148-50

[Iron-deficiency anemia as a hematological mask of myxedema].

[Article in Ukrainian]

Vydyborets' SV

An atypical course of myxedema manifested by iron-deficiency anemia is described that proved to be a diagnostic challenge. Pathogenetic mechanisms of origination are analyzed.

Eur J Endocrinol 2000 Mar;142(3):217-23

Iron supplementation in goitrous, iron-deficient children improves their response to oral iodized oil.

Zimmermann M, Adou P, Torresani T, Zeder C, Hurrell R

Human Nutrition Laboratory, Swiss Federal Institute of Technology (ETH), Zurich, Switzerland.
michael.zimmermann@ilw.agrl.ethz.ch

OBJECTIVE: In developing countries, many children are at high risk for both goiter and iron-deficiency anemia. Because iron deficiency may impair thyroid metabolism, the aim of this study was to determine if iron supplementation improves the response to oral iodine in goitrous, iron-deficient anemic children. DESIGN: A trial of oral iodized oil followed by oral iron supplementation in an area of endemic goiter in the western Ivory Coast. METHODS: Goitrous, iodine-deficient children (aged 6-12 years; n=109) were divided into two groups: Group 1 consisted of goitrous children who were not anemic; Group 2 consisted of goitrous children who were iron-deficient anemic. Both groups were given 200mg oral iodine as iodized oil. Thyroid gland volume using ultrasound, urinary iodine concentration (UI), serum thyroxine (T(4)) and whole blood TSH were measured at baseline, and at 1, 5, 10, 15 and 30 weeks post intervention. Beginning at 30 weeks, the anemic group was given 60mg oral iron as ferrous sulfate four times/week for 12 weeks. At 50 and 65 weeks after oral iodine (8 and 23 weeks after completing iron supplementation), UI, TSH, T(4) and thyroid volume were remeasured. RESULTS: The prevalence of goiter at 30 weeks after oral iodine in Groups 1 and 2 was 12% and 64% respectively. Mean percent change in thyroid volume compared with baseline at 30 weeks in Groups 1 and 2 was -45.1% and -21.8% respectively (P<0.001 between groups). **After iron supplementation in Group 2, there was a further decrease in mean thyroid volume from baseline in the anemic children (-34.8% and -38.4% at 50 and 65 weeks) and goiter prevalence fell to 31% and 20% at 50 and 65 weeks. CONCLUSION: Iron supplementation may improve the efficacy of oral iodized oil in goitrous children with iron-deficiency anemia.**

The following study sheds light on the situation faced when the patient cannot tolerate taking thyroid replacement hormone. The person experiences rapid heart beat and palpitations. This indicates that the

person is probably anemic from iron deficiency and will tolerate thyroxine when the anemia is corrected.

Mayo Clin Proc 2000 Feb;75(2):189-92

Anemia: a cause of intolerance to thyroxine sodium.

Shakir KM, Turton D, Aprill BS, Drake AJ 3rd, Eisold JF

Department of Internal Medicine, National Naval Medical Center, Bethesda, Md., 20889-5600, USA.

Usual causes of intolerance to thyroxine sodium include coronary artery disease, advanced age, untreated adrenal insufficiency, and severe hypothyroidism. **We describe 4 patients with iron deficiency anemia and primary hypothyroidism. After treatment with thyroxine sodium, these patients developed palpitations and feelings of restlessness, which necessitated discontinuation of the thyroid hormone. After the anemia was treated with ferrous sulfate for 4 to 7 weeks, they were able to tolerate thyroxine sodium therapy. Iron deficiency anemia coexisting with primary hypothyroidism results in a hyperadrenergic state.** In such patients, we postulate that thyroid hormone administration causes palpitations, nervousness, and feelings of restlessness. Correction of any existing pronounced anemia in hypothyroid patients who are intolerant to thyroxine sodium therapy may result in tolerance to this agent.

J Nutr 1998 Aug;128(8):1401-8

Plasma thyroid hormone kinetics are altered in iron-deficient rats.

Beard JL, Brigham DE, Kelley SK, Green MH

Nutrition Department, The Pennsylvania State University, University Park, PA 16802, USA.

Iron deficiency anemia is associated with lower plasma thyroid hormone concentrations in rodents and, in some studies, in humans. The objective of this project was to determine if plasma triiodothyronine (T3) and thyroxine (T4) kinetics were affected by iron deficiency. Studies were done at a near-thermoneutral temperature (30 degrees C), and a cool environmental temperature (15 degrees C), to determine plasma T3 and T4 kinetics as a function of dietary iron intake and environmental need for the hormones. Weanling male Sprague-Dawley rats were fed either a low Fe diet [iron-deficient group (ID), <5 microg/g Fe] or a control diet [control group (CN), 35 microg/g Fe] at each temperature for 7 wk before the tracer kinetic studies. An additional ID group receiving exogenous thyroid hormone replacement was also used at the cooler temperature. For T4, the disposal rate was >60% lower (89 +/- 6 vs. 256 +/- 53 pmol/h, $P < 0.001$) in ID rats than in controls at 30 degrees C, and approximately 40% lower (192 +/- 27 vs. 372 +/- 26 pmol/h, $P < 0.01$) in ID rats at 15 degrees C. Exogenous T4 replacement in a cohort of ID rats at 15 degrees C normalized the T4 concentration and the disposal rate. For T3, the disposal rate was significantly lower in ID rats in a cool environment (92 +/- 11 vs. 129 +/- 11 pmol/h, $P < 0.01$); thyroxine replacement again normalized the T3 disposal rate (126 +/- 12 pmol/h). Neither liver nor brown fat thyroxine 5'-deiodinase activities were sufficiently different to explain the lower T3 disposal rates in iron deficiency. Thus, plasma thyroid hormone kinetics in iron deficiency anemia are corrected by simply providing more thyroxine. This suggests a central regulatory defect as the primary lesion and not peripheral alterations.

[Gartner R, Dugrillon A.](#)

[From iodine deficiency to goiter. Pathophysiology of iron deficiency goiter].
Internist (Berl). 1998 Jun;39(6):566-73. Review. German. No abstract available.
PMID: 9677510; UI: 98342474

Am J Clin Nutr 2000 Jan;71(1):88-93

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Persistence of goiter despite oral iodine supplementation in goitrous children with iron deficiency anemia in Cote d'Ivoire.

Zimmermann M, Adou P, Torresani T, Zeder C, Hurrell R

Human Nutrition Laboratory, Swiss Federal Institute of Technology, Zurich, Switzerland.
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BACKGROUND: In developing countries, many children are at high risk of goiter and iron deficiency anemia. Because iron deficiency can have adverse effects on thyroid metabolism, iron deficiency may influence the response to supplemental iodine in areas of endemic goiter. **OBJECTIVE:** The aim of this study was to determine whether goitrous children with iron deficiency anemia would respond to oral iodine supplementation. **DESIGN:** A trial of oral iodine supplementation was carried out in an area of endemic goiter in western Cote d'Ivoire in goitrous children (n = 109) aged 6-12 y. Group 1 (n = 53) consisted of goitrous children who were not anemic. Group 2 (n = 56) consisted of goitrous children who had iron deficiency anemia. At baseline, thyroid gland volume and urinary iodine, thyrotropin, and thyroxine were measured by

using ultrasound. Each child received 200 mg I orally and was observed for 30 wk, during which urinary iodine, thyrotropin, thyroxine, hemoglobin, and thyroid gland volume were measured. RESULTS: The prevalence of goiter at 30 wk was 12% in group 1 and 64% in group 2. The mean percentage change from baseline in thyroid volume 30 wk after administration of oral iodine was -45.1% in group 1 and -21.8% in group 2 ($P < 0.001$). Among the anemic children, there was a strong correlation between the percentage decrease in thyroid volume and hemoglobin concentration ($r(2) = 0.65$). CONCLUSION: The therapeutic response to oral iodine was impaired in goitrous children with iron deficiency anemia, suggesting that the presence of iron deficiency anemia in children limits the effectiveness of iodine intervention programs.

Bolus of Deferoxamine Reduces Ferritin Levels in Patients With Iron Overload

WESTPORT, May 08 (Reuters Health) - Bolus injection of deferoxamine decreases serum ferritin concentrations in patients with iron overload, researchers in Italy report in the May 1st issue of *Blood*.

Dr. Massimo Franchini, of Ospedale Policlinico in Verona, and colleagues studied 27 adults with iron overload due to various conditions or treatments. Initial comparison of two doses of deferoxamine, given subcutaneously 12 hours apart, and a 12-hour subcutaneous infusion of deferoxamine showed that mean 48-hour urinary iron excretion was similar for both types of administration.

Twenty-six patients continued therapy with bolus injection, and the researchers measured serum ferritin concentrations at various times up to a mean of about 20 months. Overall, ferritin concentrations dropped from an average of 1631.5 micrograms/L to below 1,000 micrograms/L in 73% of patients, below 500 micrograms/L in 42% of patients, and to normal levels in 26% of patients.

Dr. Franchini's group notes that patients who did not receive blood transfusions during deferoxamine therapy had a significantly larger decrease in mean serum ferritin concentration compared with patients who regularly had transfusions. Ferritin concentrations did not reach normal levels in any patients who had transfusions.

The authors caution that measuring serum ferritin is not an accurate way of measuring iron stores, and that the two methods of administering deferoxamine should be compared with respect to levels of free iron.

However, they believe that the results "support the need for a prospective, randomized controlled trial in a larger and more homogenous population of patients in which hepatic, cardiac, and endocrine functions are systematically assessed."

Blood 2000;95:2776-2779.

The following study offers support for a copper deficiency in hyperthyroidism since iron has enhanced toxicity to the liver in hyperthyroidism. Low copper allows free iron which is uncoupled to copper to be more toxic.

Redox Rep 1999;4(5):243-50

Derangement of Kupffer cell functioning and hepatotoxicity in hyperthyroid rats subjected to acute iron overload.

Boisier X, Schon M, Sepulveda A, Basualdo A, Cornejo P, Bosco C, Carrion Y, Galleano M, Tapia G, Puntarulo S, Fernandez V, Videla LA

Programas de Farmacologia Molecular y Clinica, Facultad de Medicina, Universidad de Chile, Santiago.

Liver oxidative stress, Kupffer cell functioning, and cell injury were studied in control rats and in animals subjected to L-3,3',5-tri-iodothyronine (T3) and/or acute iron overload. Thyroid calorigenesis with increased rates of hepatic O₂ uptake was not altered by iron treatment, whereas iron enhanced serum and liver iron levels independently of T3. Liver thiobarbituric acid reactants formation increased by 5.8-, 5.7-, or 11.0-fold by T3, iron, or their combined treatment, respectively. Iron enhanced the content of protein carbonyls independently of T3 administration, whereas glutathione levels decreased in T3- and iron-treated rats (54%) and in T3Fe-treated animals (71%). Colloidal carbon infusion into perfused livers elicited a 109% and 68% increase in O₂ uptake in T3 and iron-treated rats over controls. This parameter was decreased (78%) by the joint T3Fe administration and abolished by gadolinium chloride (GdCl₃) pretreatment in all experimental groups. Hyperthyroidism and iron overload did not modify the sinusoidal efflux of lactate dehydrogenase, whereas T3Fe-treated rats exhibited a 35-fold increase over control values, with a 54% reduction by GdCl₃ pretreatment. Histological studies showed a slight increase in the number or size of Kupffer cells in hyperthyroid rats or in iron overloaded animals, respectively. Kupffer cell hypertrophy and hyperplasia with presence of inflammatory cells and increased hepatic myeloperoxidase activity were found in T3Fe-treated rats. It is concluded that hyperthyroidism increases the susceptibility of the liver to the toxic effects of iron, which seems to be related to the development of a severe oxidative stress status in the tissue, thus contributing to the concomitant liver injury and impairment of Kupffer cell phagocytosis and particle-induced respiratory burst activity.

IRON DEFICIENCY AND THERMOREGULATION

The following studies offer evidence that the inability to maintain body temperature (feeling cold when others are warm) is due to iron deficiency. Most hypos experience this, indicating that iron deficiency is usually a factor in hypothyroidism.

IRON DEFICIENCY AND SUPPLEMENTATION IMPACT THERMOREGULATION AND BROWN ADIPOSE TISSUE (BAT) MITOCHONDRIAL MORPHOLOGY OF RATS EXPOSED TO COLD

Author(s):

MICHELSSEN KIM G HALL CLINTON B NEWMAN JR SAMUEL M DROKE ELIZABETH A SLEEPER
MARY E LUKASKI HENRY C

Interpretive Summary:

The role that iron (Fe) plays in regulating whole-body temperature is not well defined. Fe-deficient rats have reduced concentrations of thyroid hormones and altered body temperature. Because thyroid hormones act at the mitochondria level of brown adipose tissue to produce heat, Fe status may affect the structural characteristics of mitochondria, a cell component that produces energy to maintain body temperature. To examine the relationships among dietary iron, body temperature, thyroid hormones, and brown adipose tissue mitochondria, young male rats were fed diets containing adequate or deficient amounts of Fe. Some of the rats fed the low-Fe diets then were given the diet containing an adequate amount of Fe. When exposed to cold air for four hours, the rats fed the Fe-deficient diet had a greater decline in body temperature than the rats fed the Fe-adequate diet. The rats initially fed the Fe-deficient diet then fed the Fe-adequate diet had similar body temperatures as the animals fed the Fe-adequate diet. Plasma thyroid hormone concentrations were less in the rats fed the Fe-deficient, as compared to the Fe-adequate and Fe-deficient supplemented with adequate Fe diets. The structure of mitochondria suggests that Fe deficiency produced changes that indicate impaired heat production; this change was ameliorated with Fe supplementation. These findings indicate that Fe deficiency reduces the capability of rats to maintain body temperature during short-term cold exposure. Biological impairments of Fe deficiency lie in the production of adequate amounts of thyroid hormones and adverse changes in the mitochondria that inhibit the production of heat. This information will be useful to scientists who seek to understand how mineral elements regulate energy utilization.

See also:

<http://www.nap.edu/books/0309054842/html/248.html>

IRON DEFICIENCY

Several key observations have stimulated interest in the relationship between iron deficiency and thermoregulation. Iron-deficient anemic rats were found to be unable to maintain normal body temperature when exposed to cold (39°F [4°C]) (Beard et al., 1982, 1984; Dillmann et al., 1979, 1980). Accompanying the impairment in thermoregulation were a decrease in the rate of thyroid hormone turnover and an increase in the rate of norepinephrine turnover, as compared to those observed in noniron-depleted cold-exposed (control) rats. Iron-deficient humans are unable to maintain their body temperature during exposure to cool water (82°F [28°C]) (Beard et al., 1990a; Martinez-Torres et al., 1984) or cool air (61°F [16°C]) (Lukaski et al., 1990), compared to subjects with normal iron status and equivalent body composition. Additionally, the iron-deficient subjects had lower thyroid hormone (Beard et al., 1990a) and higher catecholamine responses to cold (Lukaski et al., 1990; Martinez-Torres et al., 1984), similar to the response of iron-deficient rats. After repletion with iron supplements, the previously iron-deficient human subjects showed improved ability to maintain body temperature in the cold. These observations clearly demonstrate the link between iron deficiency and poor thermoregulation.

Anemia vs. Tissue Iron Deficiency

Iron deficiency may exert its effects on thermoregulation through two distinct, yet related, mechanisms, one involving anemia and the other involving tissue iron deficiency. Iron-deficiency anemia results in decreased oxygen transport from the lungs to tissues, and this reduction in oxygen availability inhibits physiological responses to cold, including peripheral vasoconstriction, a heat-conserving process, and increased metabolic rate, a heat-generating process. Hypoxia, created by reducing the oxygen content or the pressure of inspired air, results in hypothermia in rodents (Gautier et al., 1991). The inability to conserve and produce body heat properly accounts for hypoxia-induced hypothermia (Wood, 1991). Lack of oxygen availability for aerobic metabolism causes a decrease in metabolic

rate and, subsequently, a decrease in heat production. Hypoxic rats demonstrate decreased shivering and nonshivering thermogenesis (Gautier et al., 1991) and a decrease in body temperature set-point (Gordon and Fogelson, 1991). Impaired neural control of these processes may also account for the effects of hypoxia on thermoregulation (Mayfield et al., 1987). Tissue iron deficiency, apart from anemia, decreases the ability of muscles to utilize energy for muscular contraction, presumably via a decrease in the activity of mitochondrial iron-containing enzymes required for the oxidative production of ATP (Davies et al., 1984).

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LATEST IDEAS

Last Updated: February 11, 2001

On this page I would like to present my latest thinking on the origin and correction of thyroid disease.

It seems to me that thyroid disease is caused by deficiencies of key minerals and that there are critical steps of mineral metabolism that need to be working for normal thyroid metabolism.

The thyroid gland produces the thyroid hormone T4, which is really a pro-hormone, and T4 must be converted by a deiodinase enzyme in the liver and kidneys to T3, which is the cellularly active thyroid hormone which controls metabolic rate.

The key steps in mineral metabolism which are necessary for normal thyroid metabolism are these:

1. Several minerals are necessary for the production of thyroid hormone, T4. These minerals include iodine, iron, manganese, zinc, copper, chromium, selenium, cobalt, and possibly other ultratrace minerals. These minerals and other nutrients which work with these minerals must be in the diet or supplemented.
2. One mineral, selenium, is necessary for formation of the deiodinase enzyme which converts T4 into T3.
3. Another mineral, copper, seems to be necessary for suppressing the production of immune system malfunctions which cause autoimmune Graves' disease, and appears to have other critical functions in preventing hyperthyroidism.
4. Several minerals, including potassium, sodium, lithium, calcium, and magnesium, regulate the passage of minerals, other nutrients, and T3, through cell membranes. Imbalances of these "gateway minerals" can limit T4 production by interfering with the transport of minerals into the thyroid cells and can also limit the amount of T3 which gets into the body's cells, thereby limiting the rate of metabolism.
5. Other nutrients including vitamins, proteins, and fats which work with the minerals need to be present for the minerals to work properly to perform normal endocrine functions.

Of all these steps, perhaps the critical step is passage of key nutrients into the cells. Even if adequate minerals are in the diet, if they don't get into the cells, there will be a functional deficiency.

We have seen that balance is a key concept in understanding nutrition and the nutritional correction of disease. This seems most true when we talk about the minerals which regulate the intercellular passage of nutrients. The sodium-potassium channels, the lithium-sodium counter transport system, and the calcium channels all depend upon the ratios of minerals rather than their absolute concentrations.

In the years that I've been studying this disease I have still not seen one bit of information that suggests that hyperthyroidism and Graves' are the result of anything other than nutritional deficiencies and imbalances. When you get the right nutrients, you can feel better in hours or days.

My latest thinking is that hyperT results when there are imbalances in two key mineral relationships:

- (1) zinc/cadmium/iron/copper
- (2) sodium/potassium/calcium/magnesium

(1) Copper gets depleted by various methods: excess zinc or cadmium can deplete copper; various vitamin deficiencies, such as biotin, PABA, pantothenic acid, B-2, niacin, or B-1, can prevent copper from being utilized correctly. Therefore copper has to get replenished by supplementation (5-8 mgs per day); removing excess cadmium (smoking, chocolate, coffee, excess green leafy vegetables, etc.); removing excess zinc (stop taking multiple vitamin/mineral supplements, limit high zinc/low copper meats, limit B-6 which assists zinc metabolism), and by limiting iron and the nutrients that help iron metabolism (B-12, manganese, folic acid).

(2) Correct the imbalances in sodium/potassium/calcium/magnesium minerals. The balance of these minerals is critical since this balance controls the transport of water, other minerals, and other nutrients through the cell walls.

It appears that in hyperthyroidism, excess sodium and calcium deplete potassium and magnesium. Deficiencies of these two minerals causes wide-ranging problems. Among other problems, magnesium deficiency causes rapid heart rate and potassium deficiency causes weak or irregular heart rate.

Either potassium or magnesium will be more depleted and it's necessary to correct the deficiencies without upsetting the critical potassium/magnesium balance. To determine which mineral is more depleted, look at your symptoms. Magnesium deficiency seems to cause rapid heart rate since magnesium is involved in muscular relaxation. Magnesium deficiency prevents the heart muscles from going through a complete relaxation phase so the heart rate accelerates.

Potassium depletion not only causes irregular heart rate, but it seems to cause water to enter the cells and stay there, causing the body to swell up with edema. This is the reason why many hypers (and hypos) gain

weight--it's all water retention. If you are swelling up, then you are probably potassium deficient, so take more potassium than magnesium. If you are losing weight, then probably magnesium is more deficient than potassium, so take more magnesium than potassium.

The deficiencies of potassium and magnesium explain why sodium and calcium (dairy products, etc.) aggravate hyper symptoms, since sodium especially depletes potassium and calcium especially depletes magnesium.

There is also an interaction between the metals in group (1) and the minerals in group (2). Zinc depletes potassium and cadmium depletes magnesium. Copper assists magnesium metabolism and potassium seems essential to enable copper to get into the cells.

The interactions are probably more complex than described, but the important message is that a deficiency of one mineral has wide-ranging repercussions on the balances of other minerals. The key deficiencies are copper and its large collection of assisting nutrients, magnesium, and potassium.

Potassium is the strangest to replenish because all the supplements available are limited to 99 mgs. Our daily requirement is about 3000 mgs, so taking one or two tablets doesn't do much. You'll probably have to take 800 mgs or more a day to effect any change. It also helps to increase high potassium foods like bananas (400 mgs in one) and potatoes (500 mgs in one).

Keep in mind that excess potassium can deplete magnesium (and increase heart rate), while excess magnesium can deplete potassium (and cause irregular heart rate). Strive for a balance between these two minerals as you experiment to determine appropriate supplementation amounts. Start with small amounts and don't take a lot of one without the other. Remember that foods are the primary source of these minerals so use supplements as needed to create balance.

There are a lot more complexities involved, but this is a good summary of my present thinking about how to correct hyperthyroidism. Once the hyper phase is controlled, many people go back hypo and at this point, other nutrients may need to be added (iron, selenium, chromium, zinc, B-12, etc.) to boost thyroid production up to normal. That's a whole other story.

POTASSIUM

I have a theory that a potassium deficiency is a critical precursor of thyroid disease. The reason that it's been undetected is that both the causative and corrective process occurs so slowly that it's difficult to perceive. The theory is this:

Of the five minerals involved in the cellular transport of nutrients, potassium seems to be the most likely to be deficient in thyroid disease. The initial effects of long-term potassium deficiency cause hypothyroidism but when the deficiency gets severe, hyperthyroidism results.

Deficiencies of potassium decrease the ability of nutrients and hormones to enter the cells by disrupting the sodium/potassium transport system. This results in mineral deficiencies which then cause abnormal thyroid function, and can cause other symptoms like causing the cells to accumulate water, resulting in cellular and bodily edema. This edema or weight gain is seen in both hypothyroidism and hyperthyroidism.

Low potassium can contribute to hypothyroidism by not only preventing nutrients from getting into the thyroid cells thereby limiting production of T4, but also by limiting how much T3 can get into the cells, thereby lowering the metabolic rate of the cells and body.

It's possible that very low potassium levels are the beginning trigger of hyperthyroidism. Copper and magnesium transport into the cells decreases and this combination causes the various symptoms associated with hyperthyroidism. Magnesium deficiency decreases the ability of the heart and muscles to fully enter a relaxation phase resulting in muscular cramps and tics. These effects are seen in the heart as rapid heart rate, since the relaxation phase of the heart beat is shortened. This magnesium deficiency makes the person very intolerant of calcium intake since calcium is a natural antagonist of magnesium and is the promoter of muscular contraction.

Potassium deficiency also decreases copper transport into the cells and this results in copper-deficiency anemia, since the iron no longer has enough copper to form an adequate amount of hemoglobin. Intake of iron further depresses copper levels resulting in more hyper symptoms when iron, manganese, or cobalt are ingested.

Both hypers and hypos report that magnesium supplementation can relieve many of the symptoms of thyroid disease. Hypers in particular report that magnesium reduces episodes of rapid heart rate, which are referred to as "thyroid storms." One possibility is that the magnesium deficiency experienced in hyperT is actually a result of potassium deficiency. A high ratio of sodium to potassium may favor the transport of calcium into the cells at the expense of magnesium. This pushes the heart rate higher because of the subsequent high calcium/magnesium ratio. Magnesium supplementation helps, but perhaps the key to increasing magnesium is the use of potassium supplements along with magnesium supplements.

In my experience I've found that magnesium decreases the rapid heart rate of hyperT for a short period of

time, but does not cause any progress in the long-term goal of correcting hyperT. What does control hyperT in the long run, is supplementation with copper and the nutrients which help copper metabolism.

I've wondered what causes the copper deficiency in the first place. One possibility is that thyroid disease begins with potassium deficiency, or rather a too high a ratio of sodium to potassium over a long period of time. This results in the gradual increase in copper and magnesium deficiencies, and the serious symptoms of hyperT are the result of problems created when these nutrients get deficient.

What evidence is there that potassium deficiency is a key precursor to thyroid disease?

1. Adrenal hormones cortisol and aldosterone, which are increased during stress stimulate potassium excretion.
2. Hypokalemic periodic paralysis, a condition caused by potassium deficiency in which the body becomes rigid, is associated with hyperthyroidism.
3. The synthesis of muscle protein requires potassium and we see muscle wasting in hyperthyroidism.
4. The excessive use of salt depletes potassium and we see that hypers often have an intolerance for salt.
5. Coffee and sugar increase the excretion of potassium from the body and we've seen that decreasing or eliminating coffee and sugars, including fruits, helps hyperthyroidism recovery.
6. Physical activity increases potassium excretion and we've seen that many hypers have been exercising extensively before developing hyperT. "Extensive physical exertion for 3 hours a day can dissipate from 700 to 800 milligrams of potassium, which radiates out from sweat." (Nutrition Almanac)
7. An early symptom of potassium deficiency is decreased heart rate as you would experience in hypothyroidism. (In my experience a slow, pounding heart rate indicates potassium deficiency, while a fast heart rate indicates magnesium deficiency.)

If potassium deficiency is a causal factor in thyroid disease, then why hasn't it been discovered before now? When I had hyperthyroidism, I experimented with potassium and never experienced any effect one way or the other. However, I've recently learned that I was ignorant of some key bits of information about potassium.

First, the Nutrition Almanac states that "Potassium constitutes 5% of the total mineral content of the body." Potassium is not a trace mineral, but a major mineral. The body normally has a lot of it and requires a large intake each day to maintain adequate levels. The amount of potassium in the average person's daily diet is estimated at 2000 to 6000 milligrams, with an estimated minimum requirement of 2500 mgs. A banana contains about 450 mgs. and a potato about 600 mgs.

Second, there appears to be a law which limits the amount of potassium which can be put into a supplement at 99 mgs. This means that to satisfy your daily requirement of potassium by supplementation would require 25 capsules. When I had hyperT and experimented with potassium I was taking 1 or 2 capsules a day. This was an insignificant amount and it's no wonder that I felt no effects. If you became deficient and needed to replenish your body stores, you might have to take 10-20 capsules a day to have any significant effect.

I don't know the reason for limiting supplemental amounts of potassium to 99 mgs, but the result is that few people will ever experiment with adequate amounts to affect their conditions. If hypothyroidism is the result of long-term potassium deficiency and hyperthyroidism is the result of severe long-term potassium deficiency, who would ever find out? You would have to take what would appear to be huge amounts of potassium, and you'd also have to replenish all the nutrients that became deficient while you were potassium deficient. Experiments of this complexity just don't get done.

I think that it's worthwhile experimenting with potassium to see what effects it might have. Remember, that potassium itself is not going to relieve the major symptoms of thyroid disease—it just opens the cellular door for the important minerals to get in so they can perform their duties. Used in conjunction with the other recommended nutrients, additional potassium from supplementation or eating extra amounts of high potassium foods like potatoes and bananas may be a key in recovery.

For those who have experienced weight gain or edema, watch your weight and other symptoms. I found that when I was potassium deficient, at night when I removed my socks I saw noticeable indentation marks where my socks were. Above the sock line, my legs seemed swollen. So far, getting extra potassium has significantly reduced that symptom.

My latest hair analysis showed very low potassium levels but I ignored this evidence. While my high heart rate days of hyperthyroidism have been long gone, I started experiencing periods of very slow pounding heart rate at night. I attempted to use magnesium and copper to try to control this, and sometimes it would help. However, I reached a point where magnesium and copper only made the situation worse. In fact everything made it worse and I was at a complete loss about what might be causing those symptoms.

Finally, the symptoms got so severe that I was getting that "maybe I'm going to die feeling." One night about 3 am when I awoke with muscle cramping, severe heart problems, and I could hardly walk, I decided I had to try something that I wasn't supplementing. For some reason I tried potassium and within 20 minutes the symptoms were substantially less and within an hour I was comfortably back to sleep. Over the next two weeks, continuing potassium supplementation completely eliminated all of those heart symptoms. Another reminder that no matter how bleak a health situation might seem, when you get the right nutrient you can recover in minutes.

As I've experimented with potassium I have developed a first rule that you may want to check out for yourself: If you feel your heart rate pounding at a high rate, reach for magnesium first. If you feel your heart rate pounding at a low rate, reach for potassium first.

The ratio of potassium to magnesium seems to be important. If we need a minimum daily intake of 2500 mgs of potassium and 400 mgs of magnesium to maintain health, then perhaps a ratio of 6:1 might be appropriate. This seems high to me, but I have very little information to go by. My gut feeling is that for supplementation, it might be best to take between a 1:1 and a 2:1 ratio of potassium to magnesium. For example, try 400-800 mgs of potassium and 400 mgs of magnesium if you're experiencing pounding heart rate problems (adjust the ratio depending on whether it's a high or low heart rate). Remember to factor in your dietary intake of these minerals since the potassium content of foods can be high (450 mgs for a banana).

Persons with hyperthyroidism who want to try potassium supplementation should proceed with caution. Try a small amount and increase very gradually, making sure to take copper and magnesium as needed.

Let me know if you have any information that might be pertinent to these ideas. Thanks, John

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LITHIUM

Title

The effects of *lithium* therapy on thyroid and thyrotropin-releasing hormone.

Author

Lazarus JH

Address

Department of Medicine, University of Wales College of Medicine, Cardiff, UK.

Source

Thyroid, 8(10):909-13 1998 Oct

Abstract

Lithium is used in the prophylaxis of bipolar depressive disorder in augmentation treatment of depression and in the therapy of some cases of unipolar depression. *Lithium* affects cell function via its inhibitory action on adenosine triphosphatase (ATPase) activity, cyclic adenosine monophosphate (cAMP), and intracellular enzymes. The inhibitory effect of *lithium* on inositol phospholipid metabolism affects signal transduction and may account for part of the action of the cation in manic depression. *Lithium* also alters the in vitro response of cultured cells to thyrotropin-releasing hormone (TRH) and can stimulate DNA synthesis. *Lithium* is concentrated by the thyroid and inhibits thyroidal iodine uptake. It also inhibits iodotyrosine coupling, alters thyroglobulin structure, and inhibits thyroid hormone secretion. The latter effect is critical to the development of hypothyroidism and goiter. Effects on brain deiodinase enzymes and alterations in thyroid hormone receptor concentration in the hypothalamus are under investigation in relation to the therapeutic effect of *lithium*. The ion affects many aspects of cellular and humoral immunity in vitro and in vivo. This accounts for a rise in antithyroid antibody titer in patients having these antibodies before *lithium* administration whereas there is no induction of thyroid antibody synthesis de novo. Goiter, due to increased thyrotropin (TSH) after inhibition of thyroid hormone release, occurs at various reported incidence rates from 0%-60% and is smooth and nontender. Subclinical and clinical hypothyroidism due to *lithium* is usually associated with circulating anti-thyroid peroxidase (TPO) antibodies but may occur in their absence. Iodine exposure, dietary goitrogens, and immunogenetic background may all contribute to the occurrence of goiter and hypothyroidism during long-term *lithium* therapy. It is currently unclear whether the reported association of *lithium* therapy and hyperthyroidism are causal, although there is suggestive epidemiological evidence. Finally, *lithium* therapy is associated with exaggerated response of both TSH and prolactin to TRH in 50%-100% of patients, although basal levels are not usually high. It is probable that the hypothalamic pituitary axis adjusts to a new setting in patients receiving *lithium*.

Title

Effects of *lithium* and carbamazepine on thyroid hormone metabolism in rat brain.

Author

Baumgartner A; Pinna G; Hiedra L; Gaio U; Hessenius C; Campos-Barros A; Eravci M; Prengel H; Thoma R; Meinhold H

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Source

Neuropsychopharmacology, 16(1):25-41 1997 Jan

Abstract

The effects of *lithium* (LI) and carbamazepine (CBM) on thyroid hormone metabolism were investigated in 11 regions of the brain and three peripheral tissues in rats decapitated at three different times of day (4:00 A.M., 1:00 P.M., and 8:00 P.M.). Interest was focused on the changes in the two enzymes that catalyze: (1) the 5'deiodination of T4 to the biologically active T3, i.e., type II 5'deiodinase (5'D-II) and (2) the 5 (or inner-ring) deiodination of T3 to the biologically inactive 3'3'-T2, i.e., type III 5 deiodinase (5D-III). A 14-day treatment with both LI and CBM induced significant reductions in 5D-III activity. However, 5'D-II activity was elevated by CBM and reduced by LI, both administered in concentrations leading to serum levels comparable with those seen in the prophylactic treatment of affective disorders. The effects were dose dependent, varied according to the region of the brain under investigation, and strongly depended on the time of death within the 24-hour rhythm. The consequences of these complex effects of LI and CBM on deiodinase activities for thyroid hormone function in the CNS and also their possible involvement in the mechanisms underlying the mood-stabilizing effects of both LI and CBM remain to be investigated.

Title

Effects of *lithium* on stimulated metabolic parameters in dog thyroid slices.

Author

Tseng FY; Pasquali D; Field JB

Address

Diabetes Research Laboratory, St. Luke's Episcopal Hospital, Houston, Texas.

Source

Acta Endocrinol (Copenh), 121(5):615-20 1989 Nov

Abstract

Thyroid abnormalities may develop during chronic *lithium* therapy for affective disorders. *Lithium*, like iodide, inhibits TSH stimulation of adenylate cyclase and thyroid hormone release. The present study examined the effect of *lithium* on stimulation of intrathyroidal intermediary metabolism by several agonists. LiCl (5 mmol/l) did not inhibit basal cAMP, glucose oxidation or 32P incorporation into phospholipids in dog thyroid slices. Although LiCl inhibited TSH stimulation of cAMP, it did not abolish the hormone's effect on cAMP-dependent protein kinase. The stimulation of iodide organification, glucose oxidation or 32P incorporation into phospholipids by TSH, carbachol and

phorbol esters was not inhibited by *lithium*. This is in contrast to the effects of iodide, which inhibited stimulation of glucose oxidation and ³²P incorporation into phospholipids by various agonists. Thus, although both *lithium* and iodide inhibited TSH-stimulated cAMP formation, they act differently on intrathyroidal intermediary metabolism.

Title

Plasma concentrations of magnesium, lead, *lithium*, copper, and zinc in mentally retarded persons [published erratum appears in Am J Ment Retard 1987 Nov;92(3):271]

Author

Bruhl HH; Foni J; Lee YH; Madow A

Source

Am J Ment Defic, 92(1):103-11 1987 Jul

Abstract

The metal magnesium and the trace elements lead, *lithium*, copper, and zinc were determined by atomic absorption spectrophotometry in the plasma of 107 residents with different types of mental retardation at a state institution in Minnesota. Twenty-six staff volunteers and 29 residents with psychosocial mental retardation served as control subjects. Plasma magnesium concentrations were normal in all retarded subjects. Lead and *lithium* concentrations were below detection levels in all retarded and nonretarded subjects. Low copper concentrations were found in the plasma of retarded dwarfs and of male microcephalic subjects. The most significant finding was hypozincemia in 49 subjects with Down syndrome of both sexes and all ages. Because this finding was limited to residents with Down syndrome, a nutritional deficiency is most unlikely. The possible etiological factors of hypozincemia in Down syndrome were discussed.

Title

[Effect of *lithium* chloride on thyroid structural elements in the rat and on the balance of calcitropic hormones]

Author

Petrov NM; Semenov VV; Glumova VA

Source

Biull Eksp Biol Med, 99(6):711-3 1985 Jun

Abstract

Chronic experiments were performed to study the effect of *lithium* chloride on morphological and functional characteristics of rat thyroid and on the endocrine regulation of calcium metabolism. As a result of a prolonged exposure to low doses of *lithium* the thyroid manifests the signs of activation of tissue structures. As the *lithium* dose is raised, the thyrostatic effect of *lithium* occurs according to the mechanism similar to the Wolff-Chaikoff effect (colloid accumulation by follicles and suppression of hormones secretion into blood). *Lithium* chloride stimulates calcitonin production by C cells of the thyroid. However, the increase of the basal level of calcitonin has no substantial effect on calcium metabolism in the animals, since such an increase is accompanied by increment of the production of the physiological antagonist parathyroid hormone by the secretory cells of the parathyroid glands.

Title

[Calcitonin and parathyroid hormone secretion and calcium metabolism in patients with diffuse toxic goiter during treatment with *lithium* carbonate]

Author

Petrov NM

Source

Probl Endokrinol (Mosk), 30(1):22-6 1984 Jan-Feb

Abstract

Seventy-six patients (6 males and 70 females) with diffuse toxic goiter, stages I-II, received *lithium* carbonate as a thyrostatic drug. The drug dose ranged from 900 to 1500 g depending on the degree of the disease clinical symptoms. The treatment with lithium lasted 45 days. Before drug administration and on days 7, 15, 30 and 45 of treatment the content of triiodothyronine (T3), thyroxine (T4) and calcitonin was measured in the thyroid, that of parathyroid hormone (PTH) in the parathyroid gland, and that of thyrotropic hormone (TTH) in the pituitary. The concentration of ionized calcium in the serum, calcium excretion with urine, and tubular calcium reabsorption were measured concurrently. In patients with diffuse toxic goiter treated with *lithium*, calcium excretion with urine substantially reduced, whereas tubular reabsorption of calcium and phosphates increased. However, serum calcium concentration did not rise, remaining within normal during all the treatment periods. In the author's opinion, this was favoured by two factors: the *lithium*-induced increase in interstitial calcium absorption on the one hand and compensatory increase in PTH secretion on the other one. The decreased content of thyronines in the hemocirculation (T3, T4), a short-term elevation of TTH and calcitonin elevation in the blood and steady increase in PTH secretion were characteristic features of the time course of the hormonal parameters in patients with toxic goiter treated with *lithium*.

Title

Genistein but not staurosporine can inhibit the mitogenic signal evoked by *lithium* in rat thyroid cells (FRTL-5).

Author

Takano T; Takada K; Tada H; Nishiyama S; Amino N

Address

Department of Laboratory Medicine, Osaka University Medical School, Japan.

Source

J Endocrinol, 143(2):221-6 1994 Nov

Abstract

Long-term administration of *lithium* is one of the well-known causes of goiter. It can stimulate DNA synthesis in rat thyroid cells (FRTL-5) treated with thyroid-stimulating hormone (TSH). To investigate the mitogenic signal transduction system activated by *lithium*, *lithium*-induced DNA synthesis and Ca²⁺ influx were studied using two protein kinase inhibitors, genistein as a specific tyrosine kinase inhibitor and staurosporine as a potent inhibitor of protein kinase C. Genistein but not staurosporine blocked the DNA synthesis induced by *lithium* in TSH-primed cells but neither compound had any effect on the Ca²⁺ entry stimulated by *lithium*. Genistein clearly attenuated the phosphotyrosine content of the 175 kDa substrate in the presence of *lithium* but staurosporine failed to do so. Moreover, *lithium* could also stimulate DNA synthesis in protein kinase C down-regulated cells. These data demonstrate that *lithium* may require the activation of a particular genistein-sensitive kinase, possibly a tyrosine kinase, to induce cell proliferation. It is suggested that the phorbol ester-sensitive protein kinase C family might not participate in the mitogenic signal transduction pathway activated by *lithium*.

Title

Preliminary observation on the metabolism in spontaneous hereditary diabetic Chinese hamster (Shanyi colony).

Author

Hu M; Wu Y; Wu H

Address

Institute of Metabolism and Endocrinology, Second Affiliated Hospital, Hunan Medical University, Hunan Province, China.

Source

Chin Med J (Engl), 110(9):711-4 1997 Sep

Abstract

OBJECTIVE: To observe the changes of tissue *lithium* content and its relationship with glucose metabolism in spontaneous hereditary diabetic Chinese hamsters (SHDCH). **METHODS:** Twenty diabetic and ten normal Chinese hamsters were paired and separated randomly into four groups: controls (C), diabetics (D), controls treated with *lithium* carbonate (CT) and diabetics treated with *lithium* carbonate (DT). The *lithium* carbonate treatment was administered with drinking water containing *lithium* carbonate (0.2 mg/ml). Blood glucose levels were determined at 0, 1, 3, 5, 6th month, and insulin levels at 1, 3, 6th month. The *lithium* contents in liver, kidney and muscles were determined at the end of 6th month, using wet digestion assay and ICP-AES. Concentrations of fructosamine, lactic acid, GPT, BUN were also evaluated. **RESULTS:** The data showed that in Group D the *lithium* levels in hepatic tissue were lower than in Group C ($P < 0.05$), and *lithium* contents in kidney and muscle also decreased. In Group DT, the *lithium* contents in tissues were higher than in Group D ($P < 0.05$) and similar to Group C. Blood glucose levels and fructosamine concentrations decreased while insulin and lactic acid levels did not alter significantly. GPT and BUN levels did not change in both Group CT and Group DT. **CONCLUSIONS:** There is *lithium* deficiency in hepatic, renal and muscular tissues from diabetic Chinese hamsters. Low-dose and six-month-treatments of *lithium* carbonate can improve tissue *lithium* deficiency and glucose metabolism, and do not damage liver and kidney functions.

Title

Lithium orotate in the treatment of alcoholism and related conditions.

Author

Sartori HE

Source

Alcohol, 3(2):97-100 1986 Mar-Apr

Abstract

The subjects were 42 alcoholic patients (33 males and 9 females) who were treated with *lithium* orotate during an alcohol rehabilitation program in a private clinical setting for at least six months. They derive from a total number of 105 patients who received this treatment initially, while the remainder discontinued the treatment within six months. The data were collected from a private practice record and the follow-up varied between six months and 10 years. The 42 patients studied displayed a multitude of complaints in addition to chronic alcoholism. These included liver dysfunction, seizure disorders, headaches, hyperthyroidism, affective disorders. Meniere's syndrome, liver and lung cancers. Thirty-six of the 42 patients studied had been hospitalized at least once for the management of their alcoholism. *Lithium* orotate was given, 150 mg daily, with a diet low in simple carbohydrates and containing moderate amounts of protein and fat. In addition, calcium orotate (for hepatic involvement), magnesium orotate, bromelaine, and essential phospholipids (for cardiac problems), and supportive measures were instituted, if required. *Lithium* orotate proved useful as the main pharmacologic agent for the treatment of alcoholism. Ten of the patients had no relapse for over three

and up to 10 years, 13 patients remained without relapse for 1 to 3 years, and the remaining 12 had relapses between 6 to 12 months. **Lithium** orotate therapy was safe and the adverse side effects noted were minor, i.e., eight patients developed muscle weakness, loss of appetite or mild apathy. For these patients, the symptoms subsided when the daily dose was given 4 to 5 times weekly.(ABSTRACT TRUNCATED AT 250 WORDS)

Title

Thyroid hormone elevations during acute psychiatric illness: relationship to severity and distinction from hyperthyroidism.

Author

Roca RP; Blackman MR; Ackerley MB; Harman SM; Gregerman RI

Address

Department of Psychiatry, Francis Scott Key Medical Center, Johns Hopkins University School of Medicine, Baltimore, Maryland 21224.

Source

Endocr Res, 16(4):415-47 1990

Abstract

Acute psychiatric illness may be accompanied by transient hyperthyroxinemia. The mechanism of this phenomenon was examined by determining the role of thyrotropin (TSH) in the genesis of this state. Serial measurements of TSH, thyroxine (T4), free T4 index (FT4I), triiodothyronine (T3), and free T3 index (FT3I) were performed in 45 acutely hospitalized patients with major psychiatric disorders. Twenty-two (49%) patients exhibited significant elevations (greater than or equal to 2 SD above mean value of controls) of one or more thyroid hormone (or index) levels. Among depressed patients with elevated FT4I, TSH was higher (p less than .05) on the day of the peak FT4I than on the day of the FT4I nadir. There were significant positive correlations between psychiatric symptom severity and levels of FT4I among both depressed (p less than .01) and schizophrenic (p less than .025) patients. These data show that elevations of T4, FT4I, T3, and FT3I are common among psychiatric inpatients, especially early in their hospitalization, and that levels of thyroid hormones are correlated with severity of psychiatric symptomatology. TSH is higher early in the acute phase of illness and is not suppressed in the face of elevated thyroid hormone levels, a finding that distinguishes this phenomenon from ordinary hyperthyroidism. Elevations of peripheral thyroid hormone levels, particularly among depressed patients, may result from a centrally-mediated hypersecretion of TSH.

Title

The effects of lithium therapy on thyroid and thyrotropin-releasing hormone.

Author

Lazarus JH

Address

Department of Medicine, University of Wales College of Medicine, Cardiff, UK.

Source

Thyroid, 8(10):909-13 1998 Oct

Abstract

Lithium is used in the prophylaxis of bipolar depressive disorder in augmentation treatment of depression and in the therapy of some cases of unipolar depression. Lithium affects cell function via its inhibitory action on adenosine triphosphatase (ATPase) activity, cyclic adenosine monophosphate (cAMP), and intracellular enzymes. The inhibitory effect of lithium on inositol phospholipid metabolism affects signal transduction and may account for part of the action of the cation in manic depression. Lithium also alters the in vitro response of cultured cells to thyrotropin-releasing hormone (TRH) and can stimulate DNA synthesis. Lithium is concentrated by the thyroid and inhibits thyroidal iodine uptake. It also inhibits iodotyrosine coupling, alters thyroglobulin structure, and inhibits thyroid hormone secretion. The latter effect is critical to the development of hypothyroidism and goiter. Effects on brain deiodinase enzymes and alterations in thyroid hormone receptor concentration in the hypothalamus are under investigation in relation to the therapeutic effect of lithium. The ion affects many aspects of cellular and humoral immunity in vitro and in vivo. This accounts for a rise in antithyroid antibody titer in patients having these antibodies before lithium administration whereas there is no induction of thyroid antibody synthesis de novo. Goiter, due to increased thyrotropin (TSH) after inhibition of thyroid hormone release, occurs at various reported incidence rates from 0%-60% and is smooth and nontender. Subclinical and clinical hypothyroidism due to lithium is usually associated with circulating anti-thyroid peroxidase (TPO) antibodies but may occur in their absence. Iodine exposure, dietary goitrogens, and immunogenetic background may all contribute to the occurrence of goiter and hypothyroidism during long-term lithium therapy. It is currently unclear whether the reported association of lithium therapy and hyperthyroidism are causal, although there is suggestive epidemiological evidence. Finally, lithium therapy is associated with exaggerated response of both TSH and prolactin to TRH in 50%-100% of patients, although basal levels are not usually high. It is probable that the hypothalamic pituitary axis adjusts to a new setting in patients receiving lithium.

Title

Inhibitory effect of **lithium** on the release of thyroid hormones from thyrotropin-stimulated mouse thyroids in

a perfusion system.

Author

Mori M; Tajima K; Oda Y; Matsui I; Mashita K; Tarui S

Address

The Second Department of Internal Medicine, Osaka University Medical School, Japan.

Source

Endocrinology, 124(3):1365-9 1989 Mar

Abstract

We studied the effect of *lithium* on the release of T3, T4, and cAMP from perfused mouse thyroids and on cAMP content in thyroid pieces. *Lithium* significantly inhibited T3 and T4 release from TSH-stimulated mouse thyroids. This inhibitory effect on thyroid hormone release was dependent on the concentration of *lithium*. Under continuous stimulation with TSH and 3-isobutyl-1-methylxanthine, both cAMP release and cAMP content were significantly decreased by *lithium*. In addition, we studied the effect of lithium on (Bu)2cAMP-stimulated thyroid hormone release. T3 and T4 release was stimulated by (Bu)2cAMP in a similar way to TSH. *Lithium* significantly inhibited (Bu)2 cAMP-stimulated T3 and T4 release from perfused mouse thyroids. These results suggest that lithium inhibits the action of TSH in the thyroid gland by both suppression of cAMP production and inhibition at a step beyond cAMP generation.

Title

Influence of *lithium* and exercise on serum levels of copper and zinc in rats.

Author

C´ordova A; Escanero JF

Address

Departamento de Fisiolog´ia, Colegio Universitario de Soria, Universidad de Valladolid, Soria, Spain.

Source

Rev Esp Fisiol, 47(2):87-90 1991 Jun

Abstract

The variations in serum levels of Cu and Zn induced by exercise in rats undergoing Li therapy are determined. The results show that exercise until exhaustion leads to a reduction in the Li concentration, which is more pronounced in rats subjected to training (to 50% maximum capacity) in the week before the test. The serum levels of Zn and Cu increased significantly with exhaustion in untrained rats, while there were no significant alterations in trained rats, except for serum Zn in those not treated with Li. The modifications in serum induced by exhaustion are lower in rats treated with Li. It is likely that Li and exercise have opposite effects on the tissue distribution of the two ions studied.

Title

Red cell caesium, *lithium* and selenium in abstinent alcoholics.

Author

Corrigan FM; Besson JA; Ward

Address

Argyll & Bute Hospital, Lochgilphead, U.K.

Source

Alcohol Alcohol, 26(3):309-14 1991

Abstract

Using inductively coupled plasma source mass spectrometry, we have studied the red cell element concentrations of alcoholic subjects with different periods of abstinence before testing. We found consistently elevated red cell caesium concentrations and also reduced red cell selenium concentrations. These may represent persistent abnormalities in oxidation/anti-oxidation mechanisms, and red cell caesium in particular may be a long-term marker of alcohol dependence. Erythrocyte *lithium*, cerium and boron concentrations were also reduced in the abstinent alcoholic groups.

Does the following study mean that lithium is involved in calcium/magnesium metabolism?

Title

Role of trace elements Se and Li in drinking water on dental caries experience.

Author

Gauba K; Tewari A; Chawla HS

Address

Post Graduate Institute of Medical Education and Research, Department of Dentistry, Chandigarh, India.

Source

J Indian Soc Pedod Prev Dent, 11(1):15-9 1993 Mar

Abstract

An epidemiological survey of dental caries using modified Moller's index (1966) carried out in 483 children (aged 7-17 years) of rural areas--Talwandi Kalan, Dhanansu and Bhatian (District Ludhiana) of Punjab with almost similar F levels in their drinking water supply, similar socio-economic status, environmental factors/demographic parameters and dietary habits revealed wide variations in the prevalence and severity of dental caries. Further investigation extended to evaluate the concentrations of various trace elements Se, Li, Zn, Cu, Fe and Mn in drinking water to find out the disparity of dental caries status, revealed that the higher figures of prevalence and severity of dental caries observed in Dhanansu and Bhatian as compared to Talwandi Kalan could be attributed to the presence of Se in drinking water supply of these areas which

was not detectable in the water supply of Talwandi Kalan. On the contrary, the concentration of Li in water supply of Talwandi Kalan with low caries was found to be higher compared to that of Dhanansu and Bhatian with higher dental caries in children population.

Title

Lithium effects on calcium, magnesium and phosphate in man: effects on balance, bone mineral content, faecal and urinary excretion.

Author

Plenge P; Rafaelsen OJ

Source

Acta Psychiatr Scand, 66(5):361-73 1982 Nov

Abstract

Calcium, magnesium and phosphate metabolism was studied in *lithium*-treated patients, using a metabolic balance technique. Two groups of patients participated in the study: 1) Patients who were to start on a prophylactic *lithium* treatment, and 2) Long-term *lithium*-treated patients whose treatment was to be terminated. *Lithium* treatment produced a positive balance in both calcium, phosphate and magnesium. By continuous *lithium* treatment the effect on magnesium wore off, whereas the effect on calcium and phosphate persisted. In urine, *lithium* induced a decrease in both calcium and phosphate excretion, whereas the excretion of magnesium was increased. Bone mineral content was measured by photon absorption, and *lithium* treatment resulted in a decrease in bone mineral content occurring within the first 6 months of *lithium* treatment. In the patients, bioavailability of the Li₂CO₃ preparation was found to be about 95%, and the patients contained about one 24-h dose of *lithium* just before the next dose of *lithium* was administered.

Title

Mechanism of lithium action: in vivo and in vitro effects of alkali metals on brain superoxide dismutase.

Author

Shukla GS

Source

Pharmacol Biochem Behav, 26(2):235-40 1987 Feb

Abstract

Intraperitoneal administration of lithium (2 mEq/kg/day) was found to increase the superoxide dismutase (SOD) activity in certain brain regions after 24 hours (2 injections) and 3 days (once a day) of exposure. In vitro addition of wide range of lithium (0.1 to 8 mEq) to enzyme preparation as well activated cortical SOD activity; however, at 10 mEq concentrations an inhibition was observed. The increase in SOD activity did not appear to be region specific as under both in vivo and in vitro conditions lithium enhanced enzyme activity in all the tested brain regions. The effects of intraperitoneal administration of 2 mEq/kg *rubidium* and cesium for 24 hr (2 injections) and 6 days (once a day) were also studied on central SOD. Both the alkali metals were not found to produce any significant alteration in the cortical enzymic activity. When the in vitro effects of these monovalent alkali metals were tested, only 2 mEq *rubidium* was found to increase cortical SOD; however, cesium and potassium at similar concentration did not produce any appreciable effects. It appears from the data that lithium-induced increase in brain SOD activity is not an unspecific effect of alkali metals. SOD enzyme disposes cytotoxic superoxide radicals which, if not removed, could impair the normal functioning of cellular membrane and produce a variety of psychedelic compounds as well. The activation of central SOD by lithium would enhance the disposal process of superoxide radicals whose pathological concentrations may be present in affective disorders. The mechanism of lithium-induced activation of SOD, at present, is not known.

Title

Putative role for lithium in human hematopoiesis.

Author

Barr RD; Koekebakker M; Brown EA; Falbo MC

Source

J Lab Clin Med, 109(2):159-63 1987 Feb

Abstract

Ingestion of lithium salts increases production of neutrophil granulocytes from the bone marrow in human subjects when the concentration of the ion in blood is within the range 5 to 10 X 10⁻⁴ mol/L. Results of preliminary dose-response experiments appeared to indicate that nanomolar levels of lithium stimulated clonal proliferation of granulocyte precursors from normal bone marrow in vitro, suggesting the possibility that this element may contribute to the physiologic regulation of blood cell formation in humans. The present studies confirm that the influence of lithium on hematopoiesis is evident in vitro at concentrations equivalent to that demonstrable in normal blood (2 to 4 X 10⁻⁷ mol/L). Furthermore, such effects are not cell lineage specific, being observed also in clonogenic cultures of erythroid and eosinophil granulocyte progenitor cells, and the phenomenon attributed to lithium is a property shared with *rubidium* and cesium salts. These findings point to a role for lithium and its elemental relatives in the biophysical mechanisms involved with the control of human blood cell production.

Title

Effect of lithium on hepatic lipid peroxidation and antioxidative enzymes under different dietary protein regimens.

Author

Tandon A; Dhawan DK; Nagpaul JP

Address

Department of Biochemistry, Panjab University, Chandigarh, India.

Source

J Appl Toxicol, 18(3):187-90 1998 May-Jun

Abstract

Lithium in the form of lithium carbonate was administered at a dose level of 1.1 g kg⁻¹ food to rats fed normal (18% protein), low-protein (LP; 8%) and high-protein (HP; 30%) diets for a period of 1 month. A highly significant (53%) increase in the level of lipid peroxidation (LPO) was observed in protein-deficient rats but this increase was marginal in rats fed an HP diet (18%). Lithium treatment of rats fed a normal diet caused a marked decrease (22%) in LPO. Lithium administration to rats fed an LP diet also reduced the raised levels of LPO to the extent of 16%. Furthermore, lithium treatment normalized the HP-induced increase in the levels of LPO. The activities of glutathione peroxidase (GPx), *catalase* and superoxide dismutase (SOD) were reduced significantly in protein-deficient rats. On the other hand, an HP diet caused a decrease in SOD activity only. The activities of GPx and *catalase* were appreciably enhanced in lithium-treated rats. Lithium treatment to LP-fed rat markedly increased GPx activity and brought the decreased levels of SOD and *catalase* to within normal limits. Lithium administration to HP-fed rats did not cause any significant alteration in the activities of these antioxidative enzymes.

J Clin Endocrinol Metab 1999 Feb;84(2):499-503

Comparison of radioiodine with radioiodine plus lithium in the treatment of Graves' hyperthyroidism.

Bogazzi F, Bartalena L, Brogioni S, Scarcello G, Burelli A, Campomori A, Manetti L, Rossi G, Pinchera A, Martino E

Dipartimento di Endocrinologia e Metabolismo, Ortopedia e Traumatologia, Medicina del Lavoro, University of Pisa, Italy.

Effectiveness of radioiodine for Graves' hyperthyroidism depends also on its intrathyroidal persistence. The latter is enhanced by lithium by blocking iodine release from the thyroid. One hundred ten patients with Graves' hyperthyroidism were randomly assigned to treatment with radioiodine or radioiodine plus lithium, stratified according to goiter size (< or =40 or >40 mL) and evaluated for changes in thyroid function and goiter size, at monthly intervals, for 12 months. Cure of hyperthyroidism occurred in 33 of 46 patients (72%) treated with radioiodine and in 45 of 54 patients (83%) treated with radioiodine plus lithium. The probability of curing hyperthyroidism was higher and its control prompter ($P = 0.02$) in the radioiodine-plus-lithium group. Patients with < or =40-mL goiters had similar persistence of hyperthyroidism (13%), but lithium-treated patients had hyperthyroidism controlled earlier ($P = 0.04$). Among patients with >40-mL goiters, hyperthyroidism was cured in 6 of 15 patients (40%) treated with radioiodine alone and in 12 of 16 patients (75%) treated with radioiodine plus lithium ($P = 0.07$), and cure occurred earlier in the latter ($P = 0.05$). Goiters shrank in both groups ($P < 0.0001$), more effectively and promptly ($P < 0.0005$) in the radioiodine-plus-lithium group. Serum free T4 and T3 levels increased shortly after therapy only in the radioiodine group ($P < 0.01$). Lithium carbonate enhances the effectiveness of radioiodine therapy, in terms of prompter control of hyperthyroidism, in patients with small or large goiters. In the latter group, lithium also increases the rate of permanent control of hyperthyroidism.

Eur J Pediatr Surg 1996 Oct;6(5):301-2

Preoperative treatment of intractable hyperthyroidism with acute lithium administration.

Kauschansky A, Genel M

Department of Pediatrics, Yale University School of Medicine, Yale-New Haven Hospital, Conn., USA.

We present a 15-year-old girl with an unusual clinical course of intractable thyrotoxicosis that was resistant to thiocarbamide therapy and propranolol. Although the latter beta-adrenergic blocking agent has been used as the sole drug in the preparation of thyrotoxicosis patients for thyroidectomy, it was unsatisfactory for control of our case. In contrast, the patient's clinical response to lithium carbonate 900-1500 mg/d for 10 days was very good and no side effects were observed. This demonstrates the importance of lithium as the drug of choice in thyrotoxic emergencies and uncontrolled preoperative patients when rapid and safe inhibition of thyroid hormone secretion is required.

Clin Endocrinol (Oxf) 1996 Aug;45(2):215-23

The prevalence of affective disorder and in particular of a rapid cycling of bipolar disorder in patients with abnormal thyroid function tests.

Oomen HA, Schipperijn AJ, Drexhage HA

Immunology Department Erasmus University, Rotterdam, Netherlands.

OBJECTIVE: Cognitive and affective functioning is sensitive to changes in thyroid hormones. We have sought to determine: (1) the prevalence of thyroid function abnormalities in a psychiatric population on admission (as compared to the prevalence in a normal population), and (2) whether such thyroid function abnormalities are associated with the occurrence or development of cognitive and affective disorders. **DESIGN:** Serum was collected 2-3 weeks after hospitalization in 3 major clinics from 3756 psychiatric patients in 1987-1990, stored, and assayed in 1993 for the presence of antibodies against the TSH-receptor and thyroperoxidase (TPO-Ab) and for TSH levels. The psychiatric cohort was matched with a control population of healthy individuals living in the same area ($n = 1877$). The prevalence study was followed by a case-control study involving patients from one clinic that had routinely assigned a DSM-III-R classification to its patients. Cases were those admissions with thyroid abnormalities and three subgroups of cases were randomly formed demonstrating either TSH less than 0.4 mU/l ($n = 44$) or over 4.0 mU/l ($n = 44$), or TPO-Ab positivity ($n = 50$). Cases were compared to random controls from the same psychiatric population, viz patients without thyroid abnormalities ($n = 83$). Comparison was with respect to their psychiatric follow-up diagnosis (the investigator was blinded to the thyroid test results). **RESULTS:** Prevalence study. The percentage of patients positive for TSH-receptor-Ab was 0.26 (9/3504), for TPO-Ab was 10.0 (331/3316) and outside the TSH range of 0.4-4.0 mU/l was 10.0 ((332/3316): 5.9% (198/3316) > 4.0 mU/l and 4.1% (134/3316) < 0.4 mU/l). Abnormal total thyroxine levels were found in only 9.8% of subjects with abnormal TSH, indicating the predominantly subclinical character of the thyroid alteration. In comparison, the healthy area controls over 55 years of age showed the same prevalence of positive TPO-antibodies and TSH under 0.4 mU/l, but a higher prevalence of TSH over 4.0 mU/l. **CASE-CONTROL STUDY:** In

the case control analysis differences could not be noticed with regard to prevalences of dementia, schizophrenia or other psychiatric illnesses apart from the prevalence of affective disorders which were more prevalent in TPO-Ab positive patients and patients with a low serum TSH. Since prior use of lithium, carbamazepine, carbimazole and/or thyroxine could be a factor of importance in this association, analyses were also carried out excluding patients with such prior drug use. In these analyses affective disorders were still more prevalent in patients with a low serum TSH (particularly in males, 40% in cases vs 9% in controls, $P < 0.05$). The most significant association was however between TPO-antibody positivity (and in particular with high titre and/or with $TSH > 4.0$ mU/l) and a subgroup of the affective disorders, viz with a rapid cycling of bipolar disorder (18% in cases vs 0% in controls, $P < 0.001$). CONCLUSION: Though causal relations cannot be determined from this cross-sectional study, this admission survey found early forms of autoimmune thyroid disease, sometimes characterized only by TPO-Abs, highly significantly associated with rapid cycles of a bipolar disorder. It also found a weak association between subclinical hyperthyroidism (low serum TSH without TPO-Ab positivity) and affective disorder.

Ann Endocrinol (Paris) 1994;54(5):353-8

[Lithium therapy and hyperthyroidism: disease caused or facilitated by lithium? Review of the literature apropos of a case of hyperthyroidism preceded by transient hypothyroidism].

[Article in French]

Sadoul JL, Kezachian B, Freychet P

Service de Medecine Interne et d'Endocrinologie (I4), Hopital Pasteur, CHU de Nice.

A case of hyperthyroidism occurring in a 68 year old man receiving lithium carbonate (1 g/day) for 5 years is reported. The clinical history of the patient, treated for bipolar affective disorder, was remarkable for transient hypothyroidism followed several months later by tremor, increased free thyroxine and triiodothyronine, and decreased TSH levels which led to lithium withdrawal. Two months later, clinical and biological signs were unchanged, Tc99m-scan displayed a homogeneous and increased isotope uptake. In this setting, high levels of autoantibodies against TSH-receptor, and grade I exophthalmos and slightly ocular muscle enlargement at CT-scan favored the diagnosis of Graves' disease (perhaps facilitated by lithium therapy). Carbimazole treatment was effective in controlling hyperthyroidism. Review of the literature disclosed 44 cases of hyperthyroidism occurring in lithium-treated patients. Most of these cases concerned specific thyroid diseases, particularly with an autoimmune mechanism. There is also evidence for an actual role of lithium in increasing intrathyroid iodide pool and for an impact of lithium on the immune system. Thus, the hypothesis that lithium may trigger the development of an autoimmune thyroid disease in predisposed patients deserves further investigation.

Can J Psychiatry 1993 Dec;38(10):635-7

Regression of thyrotoxic ophthalmopathy following lithium withdrawal.

Byrne AP, Delaney WJ

Department of Psychiatry, University of Alberta, Edmonton.

The case of a bipolar patient who developed thyrotoxicosis with severe exophthalmos while on lithium therapy is described. The patient had required two surgical decompressions of the right orbit to relieve pressure, which occurred secondary to progression of the exophthalmos, and was scheduled for further surgery. Lithium therapy was discontinued because of poor compliance to the medication and intolerable polyuria. The exophthalmos improved dramatically within 72 hours of the withdrawal of lithium. A severe form of exophthalmos resulting from lithium therapy has not been described in the literature. The case described here adds to the body of information about the possible causes of thyrotoxic ophthalmopathy.

Nephron 1993;64(1):37-41

Decreased lithium clearance in patients with hyperthyroidism.

Owada A, Tomita K, Ujiie K, Akiba T, Marumo F

Second Department of Internal Medicine, Tokyo Medical and Dental University, Japan.

Lithium clearance was studied to investigate proximal tubular function in patients with hyperthyroidism ($n = 10$) and control subjects ($n = 7$). Patients with hyperthyroidism showed significantly reduced fractional excretion of lithium (FELi) compared with control subjects ($15.0 \pm 1.5\%$, $n = 10$, vs. $23.7 \pm 0.6\%$, $n = 7$, means \pm SE, $p < 0.001$). The reduced FELi of the hyperthyroid state was reversed toward control values with treatment by antithyroid drugs (12.6 ± 2.6 toward $26.8 \pm 2.5\%$ for 5 patients, means \pm SE). Tubular reabsorption of phosphate (TRP) was significantly increased in hyperthyroid patients compared with control subjects (96.1 ± 0.7 vs. $87.5 \pm 0.7\%$, $p < 0.001$), and it returned to control values after the treatment. Our data demonstrate that lithium clearance is decreased and TRP is increased in patients with hyperthyroidism, which suggests that proximal tubular reabsorption of sodium and TRP is increased in hyperthyroidism.

Am J Med 1997 May;102(5):454-8

Lithium treatment in amiodarone-induced thyrotoxicosis.

Dickstein G, Shechner C, Adawi F, Kaplan J, Baron E, Ish-Shalom S

Division of Endocrinology, Haifa Medical Center, Bnai Zion, Haifa, Israel.

PURPOSE: Amiodarone hydrochloride is an iodine-rich drug effective in the control of various tachyarrhythmias. It is known to cause refractory to thyrotoxicosis, which usually does not respond to regular antithyroid drugs. Lithium bicarbonate is a medication used to treat psychiatric disorders; it also influences thyroid production and release of hormones. We tried it in combination with propylthiouracil (PTU) for the treatment of amiodarone-induced thyrotoxicosis. **PATIENTS AND METHODS:** Twenty-one patients were studied. The first group ($n = 5$) was treated by amiodarone withdrawal only. The second group ($n = 7$) received PTU (300 to 600 mg), and the third ($n = 9$) PTU (300 mg) and lithium (900 to 1350 mg) daily. Patient selection was not randomized. The PTU + lithium group had more severe symptoms and signs of thyrotoxicosis, as well as thyroxine levels at least 50% above the upper limit of normal. They also had been on a longer course of amiodarone treatment (34.3 ± 11.9 months) than the PTU-only (11.4 ± 7.5) and the no-

treatment (7.8 +/- 4.2) groups. RESULTS: While there was no difference between the first two groups in time until recovery (10.6 +/- 4.0 versus 11.6 +/- 0.5 weeks, respectively), the group receiving lithium normalized their thyroid function tests in only 4.3 +/- 0.5 weeks ($P < 0.01$ versus both other groups). T3 levels normalized even earlier-by 3 weeks of lithium treatment. No adverse effects of lithium were encountered, and the medication was stopped 4 to 6 weeks after achieving a normal clinical and biochemical state. CONCLUSIONS: We conclude that lithium is a useful and safe medication for treatment of iodine-induced thyrotoxicosis caused by amiodarone. We would reserve this treatment for severe cases only. Further studies are needed to find out whether in patients with this troublesome complication lithium therapy could permit continuation of amiodarone treatment.

Does the following study imply that sodium is high in hypers, but lithium low? This would account for low Li-Na CTT values and perhaps lower influx of copper. In other words, an excess of sodium is causing a decrease in lithium.

Korean J Intern Med 1989 Jan;4(1):18-27

Red cell sodium and ionic fluxes in patients with hyper- and hypothyroidism.

Yoon YS, Hong KS, Cha BY, Kim YW, Lee KW, Son HY, Kang SK, Bang BK, Moon HR

To investigate the status of the Na⁺ concentrations [Na⁺]_i, K⁺ concentrations [K⁺]_i and ionic fluxes in red cells of human subjects with abnormal thyroid function, we measured the Na⁺(+)-K⁺ pump activity as well as Na⁺(+)-K⁺ cotransport (CoT), Na⁺(+)-Li⁺ countertransport (CTT) and Na⁺ passive permeability in erythrocytes of 37 normal subjects, 19 untreated hyperthyroid patients, 12 treated hyperthyroid patients and 9 hypothyroid patients with T4 replacement. The mean [Na⁺]_i value in the untreated hyperthyroidism group was significantly higher than that in the normal subjects (p less than .05), but not significantly different from that in the treated hyperthyroidism group. The mean [Na⁺]_i value in the hypothyroidism with T4 replacement group, however, was significantly lower than that in the normal group (p less than .01). We did not find any significant difference of [K⁺]_i in comparing each group. It was found that the Na⁺(+)-K⁺ pump activity in erythrocytes was significantly increased in untreated hyperthyroidism (mean; 23.4% above control, p less than 10⁻⁵), but there was no significant difference in treated hyperthyroidism and hypothyroid patients with T4 replacement. The rate constant for ouabain-sensitive Na⁺ efflux in the hypothyroidism with T4 replacement group was markedly higher than that in normal subjects (p less than .01), but not significantly different in the untreated hyperthyroidism group. We observed a significant increase of the Na⁺ CoT value in the patients with untreated hyperthyroidism as compared with that of the normal subjects (p less than .05), but there was no significant difference in the patients treated for hyperthyroidism and the hypothyroidism with T4 replacement group. However, the rate constant for Na⁺(+)-CoT in the patients with hypothyroidism with T4 replacement was significantly higher than that in normal subjects (p less than .05). We observed a marked decrease of Na⁺(+)-Li⁺CTT value in the patients with untreated hyperthyroidism versus that in the normal group (p less than .01). Passive Na⁺ permeability in the patients with untreated hyperthyroidism was markedly increased (p less than .05), and was markedly decreased in the patients with hypothyroidism with T4 replacement compared to normal subjects (p less than .01). It can be concluded from these studies that an increase in Na⁺(+)-K⁺ pump activity in the patients untreated for hyperthyroidism might then be regarded as a secondary adaptive cellular response to higher [Na⁺]_i values due to enhanced passive Na⁺ permeability, rather than a direct effect of the thyroid hormone.

Clin Physiol Biochem 1986;4(3):199-209

Intracellular sodium concentration and transport in red cells in essential hypertension, hyperthyroidism, pregnancy and hypokalemia.

Gless KH, Sutterlin U, Schaz K, Schutz V, Hunstein W

Intracellular sodium content ([Na_i]), ouabain-sensitive ('Na-K ATPase') and ouabain-insensitive ('passive permeability') sodium efflux, Na-K cotransport and Na-Li ('Na-Na') countertransport were estimated in erythrocytes in 39 control subjects, 20 patients with essential hypertension, 14 patients with hypokalemia of renal or unknown etiology, 13 hyperthyroid patients and 19 pregnant women. In normokalemic essential hypertension there was only a moderate, but significant elevation of the activity of the Na-Li countertransport system. In the group of patients with hypokalemia, there was a significant increase of [Na_i], ouabain-insensitive sodium efflux and Na-Li countertransport. In hyperthyroidism, a marked decrease of Na-Li countertransport was associated with a marked elevation of [Na_i], in pregnancy an elevation of the Na-Li countertransport with a [Na_i] 43% lower than the control values. The ouabain-sensitive sodium efflux was elevated in hyperthyroidism and hypokalemia, in which [Na_i] was increased. In the control subjects there was a positive linear correlation between ouabain-sensitive sodium efflux and [Na_i]. The sodium component of the Na-K cotransport was decreased to about one third of the unchanged furosemide-sensitive potassium component during pregnancy. Conclusions: The changes of cellular sodium metabolism in essential hypertension are of minor degree as compared to those in the other conditions studied. Cellular sodium metabolism in blood cells is influenced by thyroid hormones and metabolic disorders. Na-Li countertransport, i.e. Na-Na countertransport, seems to be involved in the regulation of [Na_i]: an increase of its activity diminishes [Na_i] (pregnancy); a decrease elevates [Na_i] (hyperthyroidism). Ouabain-sensitive sodium efflux, i.e. 'Na-K ATPase', is mainly regulated by its substrate, [Na_i].

Clin Exp Pharmacol Physiol 1998 Oct;25(10):795-9

[S](#)

Acute lithium administration impairs the action of parathyroid hormone on rat renal calcium, magnesium and phosphate transport.

Carney S, Jackson P

Faculty of Medicine & Health Sciences, University of Newcastle, New South Wales, Australia.

1. Chronic lithium (Li⁺) treatment commonly produces a state of hyperparathyroidism in humans and rat although the mechanism is unknown. 2. The present study evaluated the acute effect of Li⁺ on renal electrolyte transport, particularly Ca²⁺ and Mg²⁺ in thyroparathyroidectomized (TPTX) and intact rats. 3. The acute administration of Li⁺ significantly increased water, sodium, potassium and phosphate excretion in both TPTX and intact animals; however, Ca²⁺ and Mg²⁺ excretion was only increased in the intact group. Fractional excretion (FE) of Ca²⁺ and Mg²⁺ increased from 2.2 +/- 0.2 to 3.5 +/- 0.3% and 12 +/- 2 to 18 +/- 2%, respectively ($P < 0.01$). 4. In further experiments in TPTX rats, Li⁺ administration inhibited the usual

reduction in urine Ca^{2+} and Mg^{2+} excretion following parathyroid hormone (PTH) administration and inhibited the phosphaturia. However, supramaximal concentrations of PTH overcame this inhibitory effect. For example, an FECa of $3.8 \pm 0.2\%$ was reduced to $1.4 \pm 0.2\%$ and $1.7 \pm 0.2\%$ with maximal and supramaximal PTH concentrations, respectively, while in the presence of Li^+ an FECa of 4.0 ± 0.2 was decreased to 2.8 ± 0.2 and then $1.9 \pm 0.3\%$ with the same PTH concentrations. 5. The inhibitory effect of Li^+ was reduced with a lower plasma Li^+ concentration (0.7 ± 0.2 vs $1.6\text{--}1.8$ mmol/L). The FEMg results were comparable. 6. These results demonstrate that Li^+ directly inhibits PTH-mediated renal reabsorption of Ca^{2+} and Mg^{2+} and also blunts PTH-mediated phosphaturia. Therefore, the hyperparathyroidism in humans following Li^+ treatment may be a consequence of reduced renal Ca^{2+} reabsorption.

From a group letter: Dear John,

I believe your approach to the immune system correcting itself is our best bet from my own experience and a thought, depressive patients put on lithium run the risk of low thyroid and should be tested while taking lithium.

In previous posts I mentioned my ER reaction to a drug called Fosomax for osteoporosis. My symptoms were like that of a serious thyroid storm, but the blood test indicated a normal TSH level during this attack. This drug is a type sodium and I swear I felt like I was choking to death from salt, I drank gallons of water feeling as if it were necessary to stay alive. No one knows what happened to me medically speaking. I was then put on Paxil to render the attacks they thought to be panic, but I know better and panic attacks don't turn your eyes blood red, raise your BP 50points, Pulse 35points, skin rash, etc. for 5 to 8 hours. It would begin after I would eat, anything with a sodium content over 100mg. would set it off! I have never been so scared, I have been off of Paxil now for 2 months with no problems so far.

Sheri Lynn

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MAD COW DISEASE

Following is some fascinating information that ties mad cow disease with copper/manganese imbalances. This information makes more sense than any that I've read. This information is from Mercola.com:

Mad Cows or Mad Scientists?

THE SUPPRESSION OF ALTERNATIVE EXPLANATIONS

[E-mail to a friend](#)

By David Crowe

The smoke and flames from funeral pyres for hundreds of thousands of British cows are fading into distant memory, but the fear of this disease affecting livestock or wildlife continues to circulate the globe.

Most people do not realize that there is a non-infectious explanation for Mad Cow disease and other spongiform encephalopathies and chronic wasting diseases. This is due to the reluctance of scientists, health and agriculture bureaucrats and most of the media to question a theory that affects public health once it is active policy.

One man, Mark Purdey, has turned himself from organic dairy farmer into an amateur scientist and globe-trotting epidemiologist to doggedly continue building the major alternative theory.

The infectious theory of Mad Cow disease not only resulted in the possibly unnecessary destruction of hundreds of thousands of cows, but it diverted attention from other causes of health problems facing livestock and wildlife. It created a fear of eating beef (perhaps not entirely misplaced, but for the wrong reasons) and resulted in the circulation of tons of toxic materials from the slaughtered cows into the atmosphere. It also prevented investigations into alternative solutions to the epidemic of disease, even though these might be cheaper, more constructive and far less destructive.

The dominant belief is that Mad Cow disease (also known as Bovine Spongiform Encephalopathy or BSE) and the related diseases Scrapie in Sheep and vCJD (variant Creutzfeldt Jakob Disease) in humans are caused by a prion, a mutant protein. These semi-living beings are thought to be able to withstand temperatures that would kill the hardiest bacteria, viruses and parasites. It is believed that this allowed them to be transmitted from sheep to cows through the rendering of sheep brains into MBM (Meat and Bone Meal) protein supplements for cows.

An apparently unrelated health problem in cows that existed before Mad Cow disease was warble fly infestation. These flies lay their eggs in a cow's skin, causing health problems and reducing the value of cow hides. To combat this, in the early 1980's the British government mandated the use of heavy doses of organophosphate insecticides. These were poured in an oil-based liquid along the spinal column of cows. It was intended that they be systemic, absorbed into the cow's body, as it was believed that this was necessary to provide full and enduring protection from warble flies.

Mark Purdey was one of a handful of farmers who refused to use organophosphates (such as Phosmet) on their cows in 1982. He was concerned that the high doses would damage the health of his cows because the application was so close to the spinal column. He was also concerned about the health of people who drank milk from his cows. In 1984, Purdey won his court fight, and gained the right to use less toxic methods to combat warble fly.

When the first cases of neurological problems were reported in cows in 1985, Purdey felt that his avoidance of these pesticides had been vindicated. However, researchers and the British Government had a different idea, blaming the rapidly emerging disease on the recently postulated prion, based on the detection of protein plaques in the brains of sick cows.

Purdey started to publicly argue his theory that organophosphate pesticides were actually the cause of neurological problems, attracting some attention, and seriously annoying the British scientific establishment and government who were starting to act as if the infectious theory was fact.

Purdey noted many inconsistencies in the prion theory. Cows were supposedly infected by feeding on supplements containing the brains of sheep with Scrapie, yet Shetland Islanders had been eating potted sheep brains for centuries without similar diseases occurring. He also noted that British byproducts were exported around the world, yet the 170,000 British cases of BSE far outnumbered the total in the rest of the world. Cases of BSE had been found on organic farms with cows brought in from outside, but not on those raised from birth on the organic farms, even though organic farming rules allow restricted amounts of the suspect MBM feeds.

Other ruminants, such as goats and sheep, were not affected by Mad Cow-like diseases in England, even though they were fed MBM supplements. Conversely, several antelopes at the London Zoo and cattle at the Liscombe experimental farm developed BSE, but had never been fed MBM supplements.

When BSE was found in other countries it was in places like Bretagne in northwest France where organophosphate pesticides were first encouraged by the French government. As in the UK, BSE cases first occurred a few years after the pesticide program was initiated. The lower number of cases may be due to the lower doses used, the use of annual treatments (as opposed to twice a year in the UK) and because the program was not mandatory.

As further evidence, the decline in BSE cases in the UK began about the same time the warble fly eradication program ended.

British cases of vCJD in humans also fit the environmental theory. The disease was found in some long-term vegetarians and in humans who had never eaten cow brains. There is no good explanation of why cows could only get BSE from eating sheep brains, but humans could get it from eating only other parts of cows.

Although there was a great deal of panic, there were actually few cases in humans. Purdey noted that about 80% of the 82 cases were in rural areas, even though more than 80% of Britons live in urban areas. One cluster in the Weald district of Kent is in a hops growing area where organophosphate pesticides are used at 100 times average levels for all crops.

Purdey lobbied for government funding to test his research. Eventually, he did get a small amount, and Dr. Stephen Whatley of the University of London was able to show in a test tube that organophosphates were found to produce 3 of the 4 protein transformations required to create the mutant prion protein. A victory, but also a major defeat. The UK BSE inquiry admitted that "the door is not yet closed on the possibility that OPs [organophosphates] played a role in rendering cattle susceptible to BSE infectivity," but the infectious theory was still cast in the primary role because of the inability of Whatley to show all four transformations.

Purdey was not about to give up. He felt that there must be a co-factor that he had missed. To find it he went on a tour of places in the world where spongiform encephalopathies had existed in animals or humans for some time, collecting samples of soil and feed. In these places, where organophosphates had little or no use, he found extremely high Manganese levels and low Copper, Selenium, Zinc and Iron. He did not find this in geographically similar areas where no illness was found. The causes of this mineral imbalance varied, including acid rain, volcanic emissions, lead-free gasoline production, emissions from steel, glass, ceramic, dye and munitions manufacturing and the take-off zones of major airports.

BSE-like diseases were found in Colorado among deer and elk in an area of the front ranges where overpopulation often forced starving animals to graze on pine needles. These showed very high levels of Manganese, perhaps due to acid rain from upwind smelters. In Iceland, Purdey found Scrapie associated with similar high Manganese/low Copper soil conditions. In Slovakia the two clusters of CJD are close to ferromanganese factories and glassworks (heavy users of Manganese). These cases may well be related to the almost eradicated occupational disease known as "Manganese Madness" which occurred among miners exposed to poorly ventilated working conditions. Its symptoms and brain pathology are similar to spongiform encephalopathies.

Purdey was not just randomly testing for mineral abnormalities. Copper is a constituent of the normal prion protein, and Manganese could be a replacement when Copper is deficient, or when Manganese is present at high levels, such as in many mineral supplements for cattle. It is at this point that Organophosphates re-enter the theory. They can remove copper from the body, leaving the door open for Manganese (or other similar metals) to replace it in the prion protein. This results in a non-functional conformation of the molecule, particularly when Manganese is from the 2+ form to the oxidative 3+ and 4+ forms.

Recently, Purdey traveled to Groote Eylandt, an island north-east of Australia where 25% of the world's Manganese is currently produced. He wrote a long [detailed account](#) of his journey on his web site.

About one in thirty people in the largely aboriginal Agurugu village, where the fine mine dust regularly settles most heavily, have Groote Syndrome, a progressive neurological disease.

Researchers supported by the mining company hypothesize a genetic defect introduced by Portuguese sailors 300 years ago, even though this theory does not explain why some white mine workers also have this syndrome, nor does it explain the emergence of this syndrome since open pit mining began in the 1960s.

Purdey's theory was now multi-factorial. Organophosphates were a major factor, but the copper/manganese imbalance could be exacerbated by animal feeds or mineral supplements.

Similar situations could occur where the soil is low in the antioxidant metals and high in Manganese.

After extending the theory, David Brown, a researcher at Cambridge University performed experiments that incorporated high Manganese and low Copper conditions and was able to reproduce all four protein

changes in vitro, thus providing full laboratory confirmation that Purdey's theory is at least plausible.

At the height of the Mad Cow frenzy, the British government invited Purdey to make a detailed proposal for research funding. Predictably, after sitting on the proposal for more than a year, they rejected it, and then funded two of its reviewers for some of the studies suggested by it. A cynic might conclude that they had asked for a grant proposal solely to have Purdey reveal his arguments and thoughts in full detail, so that they could then fund some 'reliable' researchers to debunk them, without giving Purdey resources that might strengthen his arguments.

Interest in Purdey's ideas is still growing in a grass roots fashion, although slowly, and usually beneath the radar of major media outlets. Purdey has a small grant from the US Fats and Protein Research Foundation, supervised by Dr. Larry Berger of the Animal Science Lab in Urbana, Illinois. Purdey recently gave 14 lectures in Japan, some Slovakian researchers are studying the influence of Manganese and Copper on familial and sporadic cases of CJD. Some British universities are also quietly investigating in this area.

Purdey is attempting to obtain brain samples from Groote Eylandt to test for manganese and copper levels, and has persuaded one local GP there to see whether a chelating drug that removes Manganese will have beneficial effects.

Purdey is now investigating whether ultra-violet light is an additional factor in the development of SE diseases, perhaps in concert with a haze of terpenes from the pine trees that often grow at these elevations. He hypothesizes that the eyes could act as a trigger, because of their concentration of nerves exposed to light.

Purdey and other researchers have turned up many potential factors that could stimulate the development of spongiform encephalopathies and chronic wasting diseases. If some or all components of this theory prove to be valid, the solutions to these devastating diseases could be incredibly simple. It may also open new avenues of research into mental illness.

Supplementation of cattle feeds with minute amounts of copper and regulation of the manganese levels could work near miracles, at minimal cost. Chelation could be used to reduce the levels found in people or animals suffering from these illnesses. Yet, it is likely that governments and the scientific establishment will continue to concentrate their efforts almost exclusively on infectious agents and genetic defects, suppressing anybody brave enough to argue against them on this or other health issues.

Mark Purdey can be reached via his website:<http://www.markpurdey.com> **or by email to** MadCowPurdey@aol.com.

Further Reading:

[The Inquiry into BSE and variant CJD in the United Kingdom](#)

Purdey M. Ecosystems supporting clusters of sporadic TSEs demonstrate excesses of the radical-generating divalent cation manganese and deficiencies of antioxidant cofactors Cu, Se, Fe, Zn. Medical Hypotheses, 2000; 54(2), 278-306
Brown DR et al. Consequences of Manganese replacement of Copper for prion protein function and proteinase resistance. EMBO J, 2000 Mar 15; 19(6): 1180-6.

[Purdey M. The Purdey Environmental Home Page](#)

[Red Flags Weekly July 24, 2002](#)

Following is an interesting story, full of intrigue, about Mad Cow Disease, from Dr. Mercola's site:
http://www.mercola.com/2001/feb/4/insecticides_mad_cow.htm

Insecticides Cause Mad Cow Disease

Pharmaceutical interests in the UK are ignoring new scientific research that shows the insecticide used in the UK government's own warble-fly campaigns triggered the UK surge of 'Mad Cow' disease.

Latest experiments by Cambridge University prion specialist, David R. Brown, have shown that manganese bonds with prions. Other research shows that prions in the bovine spine --along which insecticides are applied-- can be damaged by ICT's Phosmet organophosphate(OP) insecticide -causing the disease.

British scientists have led the current theory that an infectious prion in bonemeal fed to cattle causes bovine spongiform disease (BSE). Infectious prions are also claimed to cause new variant Creutzfeldt-Jakob Disease (CJD) in humans -from ingesting beef. But the infectious prion theory serves to obscure a tragic chemical poisoning scandal behind the majority of BSE cases.

The new work proves that the prions can bond with manganese in animal feeds or mineral licks. These manganese prions cause the neurological degeneration seen in BSE. By a similar process, prions in human brains are damaged by lice lotions containing organophosphate. This can result in neurological diseases like CJD and Alzheimer's -later in life.

Many might be surprised to hear that organophosphates were developed by Nazi chemists during the course World War Two, as a chemical weapon nerve agent.

The marginalized research has devastating financial implications for ICI. It would provide a firm basis for litigants - who could include CJD sufferers, farmers across the world and families of the many British farmers who committed suicide during this BSE debacle.

Scientist and organic farmer, Mark Purdey gave evidence to the UK BSE inquiry, that warble fly insecticide was the cause of the disease. The scientist wheeled out to rubbish Purdy's evidence -Dr. David Ray, later turned out to have been receiving funding from the insecticide manufacturer ICI.

Purdey has been consistently denied even exploratory funding to extend his privately supported research. Yet the Purdey/Brown chemical poisoning model matches with the epidemiological spread of CJD clusters in humans. It also predicts the incidence of BSE-type diseases in animals. The accepted infectious model fits neither.

The pharmaceutical industry is all the more determined to hide the chemical source of BSE and CJD, because a spotlight on chemicals would expose the role the insecticides in Alzheimer's --another neurodegenerative disease-- that might lead to claims which would dwarf those from BSE and CJD litigants. In fact, two leading brain researchers into CJD and Alzheimer's have died in suspicious circumstances in recent years.

In the United States, the Environmental Protection Agency is already reviewing Phosmet's safety. The Centers for Disease Control in the US has recently conducted experiments on mice that confirm the organophosphate risk.

Not only is the EC beef slaughter campaign futile -because BSE disease is mostly noninfectious, but unless the underlying chemical cause is addressed, BSE will simply reappear from chemical causes. A new warble fly campaign is already underway in France using the organophosphate insecticide.

Of greater concern is that some lotions for scabies and head lice are now priming children and adults, for CJD and Alzheimer's in later life.

Bonding the Prion

Cambridge University prion biochemist, David R. Brown is dismissive of the science behind the infectious model of BSE. He terms it "a very limited amount of science by a few assumed- reputable scientists." He insists there is "no evidence an infectious agent is present in either meat or milk."

"Simple tests on udder walls of cows --which could easily detect an infectious prion-- have not been done, why I don't understand."

A number of researchers have found that organophosphate(OP) in systemic warble fly insecticide can deform the prion molecule, rendering it ineffective at buffering free radical effects in the body. Worse still, the prion is then partial to bond with manganese and become a 'rogue' prion. A chain reaction whereby rogue prions turn others to rogues also, can explain the bovine spongiform disease mechanism.

Brown showed how prion protein bonds benignly with copper, but lethally with manganese. Even natural variations in relative environmental availability of manganese versus copper can trigger prion degradation.

The CJD and BSE symptoms mirror 'manganese madness', an irreversible fatal neuro-psychiatric degenerative syndrome that plagued manganese miners in the first half of the last century

Shining A Light On Spongiform

Organic dairy farmer and peer-review-published independent scientist, Mark Purdey, says the accepted theory of transmission from BSE-infected cattle to human CJD -by bonemeal or meat, is dependent on a mutant prion that has never been isolated under the scientific protocol called Koch's postulates.

Purdey's insistence on sticking to the letter of this scientific law earned him the condemnation of UK officialdom when he first mooted his theory. But Purdey pointed to CJD clusters downwind of a British Phosmet production plant to back his case.

He gave evidence to the UK Government BSE inquiry and was supported by Conservative MP, Thessa Gorman. His views were discounted, but his subsequent research and the new Cambridge prion work have confirmed the alternative theory. Despite this, and the backing of a British peer, he is denied even exploratory funding.

Why does CJD degeneration in humans begin in the retina, and why are CJD disease clusters found in high altitude locations?

The prion molecule has a known natural role as a shock absorber of damaging energy from ultraviolet rays and other oxidizing agents.

Once this prion defense system is rendered ineffective by organophosphates - for example in human head lice lotions, these oxidizing effects have an unmediated impact on tissues. Eventually, UV radiation damages the retina and oxidative stress destroys the brain tissues of CJD patients. This theory would expect to find higher CJD incidence in mountain regions -where UV radiation levels are elevated. That prediction holds true.

A similar but accelerated mechanism could be driving BSE. ICI's Phosmet organophosphate warble fly insecticide - applied on the backs of animals along the spinal column, similarly degrades prions. "Systemic versions of the insecticide are designed to make the entire cow carcass toxic to warble fly," explains Purdey. "Unfortunately it's toxic to prions too -especially those prions located just millimeters from the point of application."

The damaged prions are then ready to react with manganese in animal feed, or manganese sprayed on land or in mineral licks -to become the driving force of BSE neurodegeneration. Purdey says manganese-tipped prions set off lethal chain reactions that neurologically burn through the animal.

Chickens notoriously excrete most of the supplements fed to them -including manganese. And their manganese-rich excreta have been blended into cattle feed in the UK. Natural variations in the relative environmental availability of copper and manganese can also spur prion degeneration says Purdey.

From this research, any prudent person would conclude there is a significant risk attaching to the use of organophosphate in humans. Preparations for head lice and scabies are known to be overused in practice and might be priming users for CJ disease.

The Money Trail

Critical scientists like Purdey are unlikely to prevail. The pharma industry holds most research purse strings, and would hardly energetically explore an avenue of research that could expose them to litigation for causing BSE. The official theory is lavishly funded, alternative theories rarely, if at all.

There are more explosive implications to his -and other's latest research. Purdey says similar organophosphate-induced protein deformation could also underlie Alzheimer's disease. If that were true, the litigation fallout would destroy some pharmaceutical giants, and a lot of very influential noses would be out of joint.

Disturbingly, Purdey and other brain researchers seem to have had an undue share of unfortunate accidents. Purdey's house was burned down and his lawyer who was working with him on Mad Cow Disease was driven off the road by another vehicle and subsequently died. The veterinarian on the case also died in a car crash -locally reported as: 'Mystery Vet Death Riddle.'

Dr. C. Bruton, a CJD specialist --who had just produced a paper on a new strain of CJD-- was killed in a car crash before his work was announced to the public. Purdey speculates that Bruton might have known more than what was revealed in his last scientific paper.

In 1996, leading Alzheimer's researcher Tsunao Saitoh, 46 and his 13 -year-old daughter were killed in La Jolla, California, in what a Reuters report described as a "very professionally done" shooting.

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MAGNESIUM

Because of the competing nature of calcium and magnesium, excessive calcium intake from foods or supplements can lead to a magnesium deficiency. The symptoms of magnesium deficiency are identical with many of the symptoms of thyroid disease, especially hyperthyroidism. People of Asian descent who get hyperthyroidism often become completely rigid and may be found lying in the streets this way. The condition is called hypokalemic periodic paralysis and is highly associated with hyperthyroidism. It's possible that the origin of the disease is not from low potassium (hypokalemia) but from low magnesium, which we know is a factor in hyperthyroidism.

Functions:

The principal function of magnesium that is critical in thyroid disease is that it enables muscles to relax. With inadequate magnesium, the muscles cramp. When this happens to the heart muscles the heart does not go through a complete relaxation phase, and the next calcium-driven contraction begins before the relaxation is complete. This results in rapid heart beat and irregular heart rate known as arrhythmia.

Deficiency Effects and Symptoms:

According to the Nutrition Almanac, "Magnesium deficiency can easily occur because magnesium is refined out of many foods during processing. Cooking food removes the minerals; the oxalic acid in foods like spinach and phytic acid found in cereals bind magnesium in the body, as do unbalanced amounts of salts....A deficiency can occur in people with diabetes, those who use diuretics or digitalis preparations, the elderly, those with pancreatitis, chronic alcoholism, kwashiorkor, pregnancy, cirrhosis of the liver, arteriosclerosis or kidney malfunction, those on low-calorie or high-carbohydrate diets, and those who have severe malabsorption such as that caused by chronic diarrhea or vomiting....Fluoride, high zinc levels, high levels of vitamin D, diuretics, and diarrhea will cause a deficiency of magnesium."

Also from N. A.: "Magnesium deficiency is thought to be closely related to coronary heart disease, including myocardial necrosis. An inadequate supply of this mineral may result in the formation of clots in the heart and brain and may contribute to calcium deposits in the kidneys blood vessels, and heart. Heart failure resulting from fibrillation and lesions in the small arteries is linked to a deficiency of magnesium, as is vasodilation, which is followed by hyperkinetic behavior and fatal convulsions."

"Symptoms of a deficiency may include gastrointestinal disorders, irregular heart rhythm, lack of coordination, muscle twitch, tremors, weakness, apprehensiveness, personality changes, disorientation, confusion, depression, and irritability. A deficiency interferes with nerve and muscle impulses. Long-term deficiency can lead to tetany as in a calcium deficiency, alcoholic hallucinations, unusual face and eye movement, alopecia (baldness), swollen gums, and lesions of the gums."

Beneficial Effects:

N.A.: "Magnesium is vital in helping prevent heart attacks....After a heart attack, it has been found that supplementation provided a much higher survival rate and showed far less life-threatening dysrhythmias....It has also proved beneficial in the treatment of neuromuscular disorders, nervousness, tantrums, depression, sensitivity to noise, and hand tremor....Supplementing helps control dizziness, muscle weakness, twitching, heart disease, and high blood pressure,....reduce blood cholesterol and keep the arteries healthy....used for controlling convulsions in pregnant women, premature labor, and epileptic seizures."

Chocolate is a good source of magnesium and has a high magnesium to calcium ratio (about 4:1). Magnesium is low in hypers and the craving for chocolate may be driving my a need for magnesium. Unfortunately, chocolate may also be high in cadmium which is a probably negative factor for hyperT. Thus the craving for magnesium, if satisfied by eating chocolate, could exacerbate the symptoms of hyperT.

In this first study we see that magnesium is depleted in the hyperthyroid state and treatment by Methimazole increases the magnesium content of both erythrocytes (red blood cells) and serum. This emphasizes the need for magnesium supplementation in hyperthyroidism.

Title

Magnesium metabolism in hyperthyroidism.

Author

Disashi T; Iwaoka T; Inoue J; Naomi S; Fujimoto Y; Umeda T; Tomita K

Address

Third Department of Internal Medicine, Kumamoto University School of Medicine, Japan.

Source

Endocr J, 43(4):397-402 1996 Aug

Abstract

Changes in magnesium metabolism, along with those in sodium, were investigated in 17 patients with Graves' disease (14 females and 3 males, mean +/- SD, 44.8 +/- 12.2 years) and their relationship to plasma levels of thyroid hormones were assessed before and after treatment. Each patient was studied in hyperthyroid state and euthyroid state after treatment. Each patient was studied in hyperthyroid state and euthyroid state after treatment with methimazole. Treatment with methimazole increased the magnesium concentration both in erythrocytes (2.00 +/- 0.18 vs. 2.08 +/- 0.24 mmol/l cells, P < 0.05) and in serum (0.72 +/- 0.12 vs. 0.84 +/- 0.11 mmol/l, P < 0.001) but both urinary output and fractional excretion of magnesium decreased significantly (P < 0.05).

and $P < 0.001$, respectively). The erythrocyte sodium concentration decreased with treatment (10.7 ± 2.6 vs. 8.1 ± 1.1 mmol/l cells, $P < 0.001$) but the serum sodium remained unchanged (140.9 ± 1.9 vs. 140.9 ± 2.1 mmol/l, NS). Urinary excretion of sodium also decreased with treatment ($P < 0.05$), but only changes in indices of magnesium metabolism (decrease in renal fractional excretion, rise in serum level) correlated significantly with those of the thyroid functions with treatment. **These observations clearly indicate that in Graves' disease, the magnitude of magnesium metabolism alteration is closely related to the extent of the increase in thyroid hormones in plasma.**

This second study examines the effect of magnesium on the sodium-potassium pump in the heart. Magnesium deficiency is demonstrated to leave the number of pumps unaltered but to decrease the activity of the pumps. This appears to result in an increase of sodium inside the cells with consequent arrhythmias in the heart. This is evidence that supplementing magnesium can control rapid and irregular heartbeat experienced in hyperthyroidism.

Title

Effects of dietary magnesium on sodium-potassium pump action in the heart of rats.

Author

Fischer PW; Giroux A

Address

Nutrition Research Division, Health and Welfare Canada, Ottawa, Ontario.

Source

J Nutr, 117(12):2091-5 1987 Dec

Abstract

Sprague-Dawley rats were fed a basal AIN-76 diet containing 80, 200, 350, 500 or 650 mg of magnesium per kilogram of diet for 6 wk. Ventricular slices, as well as microsomal fractions, were prepared from the hearts and were used to determine sodium-potassium pump activity. Sodium-potassium pump activity was assessed in the microsomal membranes by determining the ouabain-inhibitable Na^+ , K^+ -ATPase activity and $[^3\text{H}]\text{ouabain}$ binding, and in the ventricular slices, by determining ouabain-sensitive ^{86}Rb uptake under K^+ -free conditions. The ATPase activity increased with increasing dietary magnesium, so that in the hearts of those animals that were fed 500 and 650 mg of magnesium/kg diet, it was significantly greater than the activity in the hearts of the animals fed 80 and 200 mg/kg diet. Similarly, ^{86}Rb uptake by heart slices from rats fed 500 and 650 mg of magnesium/kg diet was significantly greater than the uptake by heart slices from animals fed 80 and 200 mg/kg diet. $[^3\text{H}]\text{Ouabain}$ binding did not change with increasing dietary magnesium. **Thus, magnesium deficiency appears to have no effect on the number of sodium-potassium pump sites, but does decrease the activity of the pump. It is suggested that this leads to an increase in intracellular Na^+ , resulting in a change in the membrane potential, and may contribute to the arrhythmias associated with magnesium deficiency.**

The following study suggests that boron is essential for proper magnesium metabolism. Also, this study may shed light on why fructose increases the severity of a copper deficiency--it causes adverse effects when magnesium is low.

Magnes Res 2000 Mar;13(1):19-27

Magnesium deficiency in the rat: effects of fructose, boron and copper.

Kenney MA, McCoy JH

School of Human Environmental Sciences, University of Arkansas, Fayetteville 72701, USA.
kenney@comp.uark.edu

Magnesium (Mg) participates in many biochemical reactions which involve a variety of other nutrients. To elucidate some nutrient interactions, fructose (FR) and starch (ST) were compared as carbohydrate sources, and boron (B) and copper (Cu) were added to low-Mg diets for young male rats. Lack of Mg always caused characteristic deficiency symptoms. FR resembled Mg deficiency in effects on body, liver, and kidney weights and on plasma cholesterol level, but did not affect serum Mg or calcium (Ca). FR effects apparently were not mediated by changes in plasma Mg and Ca concentrations and were not prevented by adding Cu. B appeared to lessen effects of a low-Mg diet on body growth, serum cholesterol, and ash concentration in bone, but exacerbated deficiency symptoms, without affecting the concentration of Mg or Ca in serum. Results suggest that increased FR intake and marginal B might adversely affect individuals whose Mg status is suboptimal.

In the following study we see that nearly half of patients complaining of chronic fatigue symptoms and fibromyalgia (companion diseases to hypothyroidism) have magnesium deficiencies.

Magnes Res 1997 Dec;10(4):329-37

Magnesium deficit in a sample of the Belgian population presenting with chronic fatigue.

Moorkens G, Manuel y Keenoy B, Vertommen J, Meludu S, Noe M, De Leeuw I

Department of Internal Medicine, University Hospital, Antwerp, Belgium.

97 patients (25 per cent males, ages ranging from 14 to 73 years, median 38 years) **with complaints of chronic fatigue (chronic fatigue syndrome, fibromyalgia or/and spasmophilia)** have been enrolled in a prospective study to evaluate the Mg status and the dietary intake of Mg. An IV loading test (performed following the Ryzen protocol) showed a **Mg deficit in 44 patients**. After Mg supplementation in 24 patients, the loading test showed a significant decrease ($p = 0.0018$) in Mg retention. Mean values of serum Mg, red blood cell Mg and magnesuria showed no significant difference between patients with or without Mg deficiency. No association was found between Mg deficiency, CFS or FM. However serum Mg level was significantly lower in the patients with spasmophilia than in the other patients.

PMID: 9513929, UI: 98175116

The following study also shows that fibromyalgia is associated with magnesium deficiency. Very importantly it also indicates that magnesium deficiency may be a consequence of thiamine (vitamin B-1) deficiency and that selenium status is slightly correlated with magnesium levels. This shows that there is some interdependence of selenium and magnesium and that thiamine may be critical for magnesium metabolism and possibly selenium metabolism.

Magnes Res 1994 Dec;7(3-4):285-8

Selenium and magnesium status in fibromyalgia.

Eisinger J, Plantamura A, Marie PA, Ayavou T

Centre Hospitalier de Toulon, France.

Muscle pain has been associated with magnesium (Mg) and selenium (Se) deficiency: magnesium and selenium status were investigated in fibromyalgia (FM). Erythrocyte (E), leucocyte (L) and serum (S) magnesium, serum selenium and zinc, and vitamin B1, B2, A or E status were assessed in 22 patients with fibromyalgia and in 23 age-matched healthy controls. LMg is significantly increased ($P < 0.05$) and EMg slightly decreased in fibromyalgia. **These magnesium abnormalities are associated with previously-reported impairment of thiamin metabolism.** Antioxidant status (as well as plasma malondialdehyde) is unchanged in fibromyalgia and **serum selenium levels, slightly but not significantly correlated with serum magnesium**, is normal.

PMID: 7786692, UI: 95306266

The following study indicates that riboflavin (vitamin B-2) is not involved in magnesium metabolism.

Magnes Res 1993 Jun;6(2):165-6

Absence of correlation between magnesium and riboflavin status.

Eisinger J, Clairet D, Brue F, Ayavou T

Department of Rheumatic Diseases, Centre Hospitalier, Toulon, France.

Erythrocyte magnesium and glutathione reductase activity coefficient (EGR-AC), reflecting vitamin B-2 status, were assessed in 11 athletes, 20 patients with fibromyalgia, 18 patients with hypothyroidism, and 13 controls. No correlation was demonstrated between erythrocyte magnesium and EGR-AC.

PMID: 8274362, UI: 94100069

Subj: [hyperthyroidism] Re: InsomniaAnxiety

Date: 3/22/00 7:29:13 PM Pacific Standard Time

From: ramathomas@cco.net (Mary Ann Thomas)

Reply-to: hyperthyroidism@egroups.com

To: hyperthyroidism@eGroups.com

Cire, You mention that you take 300mg of magnesium with 600mg of calcium and there is a bit of talk surrounding whether or not these two should be supplemented in a 2 to 1 ratio or 1 to 1 ratio. I think John recommends something closer to a 1 to 1 ratio and I would like to share my personal experience with calcium and magnesium supplementation. I recently saw a Naturopath Physician who had me taking calcium and magnesium in a ratio higher than two to one (I can't remember the exact ratio right now). At this higher than recommended ratio I began having trouble sleeping. Most nights I couldn't get to sleep and when I did I would wake up a couple of hours later and be awake for several hours. My back and neck also started giving me more problems than normal. I had eye twitches and readily pulled muscles just from sleeping! My thyroid grew to four times it's "normal" size. When I finally reviewed my supplement list and discovered the imbalance in the calcium and magnesium ratios I adjusted my ratio back to one to one and all the above problems were alleviated including getting a full nights sleep. I currently take 1200mg of magnesium to 600mg of calcium and find that works about best for me. Perhaps you should consider

raising your magnesium.

Good Health to All!

MA

Subj: [hyperthyroidism] Re: Insomnia/Anxiety

Date: 3/22/00 8:14:20 PM Pacific Standard Time

From: mrej@centurytel.net (Cire)

Reply-to: hyperthyroidism@egroups.com

To: hyperthyroidism@eGroups.com

Mary, i think you're right. I mixed a teaspoon of Epsom salts in water and drank it this afternoon. I noticed i started to yawn and feel better.

I took another dose at dinner time and once again it seemed like it helped.

I will be looking into taking more magnesium. I know the plants like it so maybe there's a link here? Wouldn't it be something if it was as simple as magnesium deficiency? Thanks to all for the support and insight, I really appreciate it.

Cire

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MANGANESE (Mn)

Manganese is called the "maternal mineral" because manganese deficiency in females causes a reduced maternal caring for her young. Mn is necessary for the production of manganese superoxide dismutase, one of the key antioxidants in the body. Enzymes involved in cholesterol synthesis are manganese dependent, so a manganese deficiency can decrease sex drive. Mn is required for normal thyroid and adrenal gland activity.

Manganese seems to work with iron and is therefore necessary for proper iron metabolism. Excessive iron or copper supplementation can decrease manganese and excessive manganese can deplete iron and copper. Therefore it is important to supplement manganese (and it's partner chromium) when supplementing iron and copper.

NUTRITION ALMANAC INFORMATION

Manganese is essential for the formation of thyroxine. Necessary for vitamin K production. "Manganese given to older schizophrenic patients to lower copper levels sometimes results in a rise in blood pressure." Manganese deficiency can cause dizziness, ear noises, and deafness. Manganese helps treat myasthenia gravis (failure of muscular coordination and loss of muscle strength). Important in the treatment of multiple sclerosis and diabetes. Manganese is effective in increasing copper excretion from the body. Pg.124

DEFICIENCY DISEASES

Hypothyroidism, ataxia (muscle coordination failure), deafness, convulsions, chondrodystrophy, asthma, retarded growth, infertility, miscarriages, loss of libido in females and males, skeletal defects, disruption of fat and carbohydrate metabolism, joint problems (including TMJ, slipped tendon, repetitive motion syndrome, and carpal tunnel syndrome), osteoporosis, ringing in ears, dizziness, fatigue, myasthenia gravis, allergies, hypoglycemia, diabetes.

MANGANESE EXCESS SYMPTOMS

Anorexia, ataxia, iron deficiency, copper deficiency, neurological symptoms, schizophrenia, criminal behavior

GOOD FOOD SOURCES

Blueberries, ginger, rice, egg yolks, green vegetables, legumes, nuts, bananas, olives, avocados, kelp, tea

ANTAGONISTS

Iron, copper, tranquilizers.

STUDIES:

The following study indicates that if manganese is extremely low, the conversion of T4 to T3 will be accelerated by increased 5'D-I activity, leading to higher blood levels of T3.

Biol Trace Elem Res 1996 Oct-Nov;55(1-2):137-45

The effect of manganese supply on thyroid hormone metabolism in the offspring of manganese-depleted dams.

Eder K, Kralik A, Kirchgessner M

Institute of Nutrition Physiology, Technical University Munich, Freising, Germany.

The present study was performed to investigate the effect of manganese (Mn) supply on metabolism of thyroid hormones in the rat. A study with rats was carried out over two generations. Female rats were raised with a Mn-deficient diet (0.1 mg Mn/kg), and mated to produce a second generation. The male rats of the second generation were used as subjects for the investigation. They were divided into five groups and fed diets with Mn concentrations of 0.1, 0.5, 2.2, 10, and 46 mg/kg for 40 d. For assessment of thyroid hormone metabolism, concentrations of thyroid hormones in serum and activity of hepatic type I 5'deiodinase (5'D-I) were measured. Feeding diets with 0.1 mg Mn/kg impaired growth and food conversion, influenced parameters of thyroid hormone metabolism, and changed some clinical-chemical parameters, such as concentrations of total protein, albumin, calcium (Ca) and magnesium (Mg) as well as activity of alkaline phosphatase in serum. **Regarding the thyroid hormone metabolism, rats fed the diet with a Mn level of 0.1 mg/kg had a higher 5'D-I activity in liver, and consequently a higher concentration of triiodothyronine in serum than the rats fed the other diets.** In contrast, the concentrations of total and free thyroxine were not influenced by the Mn intake. Growth, clinical-chemical parameters, concentrations of thyroid hormones in serum, and activity of hepatic 5'D-I were similar in the rats fed diets with Mn concentrations between 0.5 and 64 mg/kg. The present study shows that feeding a diet with a very low Mn concentration affects growth and thyroid hormone metabolism and that a dietary level of 0.5 mg Mn/kg is adequate for growth and thyroid hormone metabolism in the offspring of Mn-depleted dams.

PMID: 8971361, UI: 97126446

Manganese ion as a goitrogen in the female mouse.

Kawada J, Nishida M, Yoshimura Y, Yamashita K

Effect of excessive ingestion of manganese (Mn) on the mouse thyroid was assessed under the conditions of normal intake of iodide. **Female mouse thyroids were enlarged after 7 weeks of administration of 200 mg/l MnCl₂ X 4H₂O in drinking water; 2.74 +/- 0.25 mg for control (N = 56), and 3.31 +/- 0.28 mg for Mn-treated group (N = 85) (p less than 0.001). In contrast, male mouse thyroids never became goitrous following this treatment. Manganese was goitrogenic to the castrated male mouse, but it had no effect on the testosterone-treated castrated male mouse, indicating the involvement of androgen in goiter formation.** Oral administration of Mn did not severely affect blocked T/S of 125I or iodine metabolism in the thyroid. A morphological study, however, revealed that the epithelial cell in the Mn-treated mouse thyroid became flatter than that of the control. The lumens were filled with colloid in Mn-treated female mouse thyroid. The serum levels of thyroxine (T₄), but not triiodothyronine (T₃), were slightly reduced by Mn. **These informations suggest that Mn can be a mild goitrogen for the female mouse and that the etiology of goiter formation can be interpreted by retention of colloid in the lumen.**

PMID: 4092670, UI: 86135843

Arch Toxicol 1983 Nov;54(3):243-6

Effects of manganese ions on thyroid function in rat.

Buthieau AM, Autissier N

Rats were treated with MnSO₄, H₂O (1 mg/100 g/day, SC) for a period of 5 weeks. Thyroxine (T₄) and triiodothyronine (T₃) levels were measured in thyroid by radioimmunoassay. T₄, T₃ and thyroid-stimulating hormone (TSH) levels were also estimated by radioimmunoassay in serum. **Manganese treatment produced no change in thyroid T₄ and T₃ levels but induced a significant decrease in serum T₄, T₃ and TSH levels.** This decrease can be interpreted as the result of a pituitary alteration which appears to be related to the high accumulation of manganese in the pituitary gland.

: Endokrynol Pol 1993;44(1):57-63

[Effect of occupational environment containing manganese on thyroid function].

[Article in Polish]

Misiewicz A, Radwan K, Karmolinski M, Dziewit T, Matysek A

VI Katedra i Klinika Chorob Wewnętrznych Śląskiej AM, Katowicach.

Significantly lower blood serum concentrations of triiodothyronine (T₃) and thyroxine (T₄) accompanied by a significantly higher concentration of thyrotropin (TSH) have been found in workers exposed to the environmental presence of manganese, iron chromates and other agents as compared to the control group (differing with respect to the environmental exposure to manganese only)

Br J Nutr 1979 Mar;41(2):253-61

Trace nutrients. 2. Manganese in British food.

Wenlock RW, Buss DH, Dixon EJ

1. The amount of manganese in nationally-representative samples of prepared and cooked groups of foods, and in a wide variety of individual foods, was determined by atomic absorption spectroscopy. 2. **The average British diet was calculated to provide 4.6 mg Mn/d of which half was derived from tea and other beverages, 30% from cereals, and 15% from vegetables and fruit. Animal products provided little Mn.** 3. **Individual foods other than tea which were particularly rich in Mn in Britain were unrefined and partially-refined cereals, and some spices and herbs. Some vegetables and fruit, coffee, wine, chocolate and brown sugar also contained significant amounts of Mn.**

PMID: 427078, UI: 79145327

Am J Clin Nutr 1983 Dec;38(6):936-42

Tea and coffee as sources of some minerals in the New Zealand diet.

Gillies ME, Birkbeck JA

Daily intakes of tea and coffee of a representative sample of adult New Zealanders (865 men and 1100 women) were calculated from 24-h dietary recalls. The mineral concentrations in tea and coffee samples were determined by atomic absorption spectrometry and used to estimate daily mineral intakes from these beverages. More than 80% consumed tea and about 60% consumed coffee on the day of the recall. The men drank significantly more tea than the women (p less than 0.001), but coffee intakes were similar. **The results indicate that for New Zealand adults tea is a very good source of manganese and it also contains appreciable amounts of potassium. Coffee is a better source of potassium than tea, has appreciable amounts of magnesium, and may contribute significantly to manganese intakes in some instances.** The amounts of copper, zinc, sodium, calcium, and iron extracted from tea leaves and coffee beans in the brewing processes are too low to be of any nutritional significance but minerals in the water used in their preparation may make a significant contribution to dietary intakes.

PMID: 6650450, UI: 84076931

The following study may be extremely significant for the understanding of Graves' disease and Graves' ophthalmopathy (TED). While I hesitate to jump to conclusions, this study seems to indicate that manganese superoxide (MnSOD), which is an antioxidant, may stimulate retroocular fibroblast growth which is the root of TED. The retroocular fibroblasts seem to grow in response to stimulation by the TSH receptor antisera

(anti-p1). MnSOD has a similar structure to the TSH receptor peptide and apparently in Graves' there is an autoimmune response to MnSOD. Therefore it is possible that an excess amount of manganese in the diet causes excessive production of MnSOD which in turn causes an autoimmune response to MnSOD and this stimulates the retroocular fibroblasts. While this would be very interesting, I don't know if my interpretation of this is correct. However, this does fit in with the fact that manganese is a copper antagonist and high levels of manganese would suppress copper levels. Copper supplementation could, in turn, help reduce manganese levels and help suppress this autoimmune response.

Immunodetection of manganese superoxide dismutase in cultured human retroocular fibroblasts using sera directed against the thyrotropin receptor.

Burch HB, Barnes S, Nagy EV, Sellitti D, Burman KD, Bahn RS, Lahiri S

Endocrine-Metabolic Service, Kyle Metabolic Unit, Walter Reed Army Medical Center, Washington, DC 20307-5001, USA.

The identification of antigenic targets in the retroocular autoimmune response of Graves' ophthalmopathy is likely to increase our understanding of mechanisms underlying this disorder. While a number of putative autoantigens have been identified on the basis of molecular weight or cell of origin, a determination of the significance of these antigens is contingent upon an identification of the amino acid sequence. Our group has previously identified **immunoreactive retroocular fibroblast (ROF) proteins recognized by thyrotropin receptor (hTSH-R) antisera (anti-p1)**, at molecular weights of 95, 71, 41, and 14-25 kDa. In the present study, proteins detected by anti-p1 and visualized by Ponceau staining were isolated and processed for microsequencing. Ponceau staining revealed dense bands at molecular weights of 14 and 23 kDa, and a weak band at 41 kDa. N-terminal sequencing was performed on the prominent band at approximately 23 kDa, showing it to be manganese superoxide dismutase (MnSOD), a mitochondrial enzyme responsible for protection against oxygen free radical-associated cellular damage. **Sequence comparison of MnSOD to the hTSH-R peptide, p1, revealed a linear segment of amino acid homology.** Preincubation of anti-p1 with p1 blocked immunodetection of the 23 kDa band corresponding to MnSOD, and immunoprecipitation of ROF protein using anti-p1 yielded protein recognized by anti-MnSOD. **Autoimmunity against human recombinant MnSOD was further assessed by ELISA. Patients with Graves' disease (n = 53) had significantly higher ELISA indices than normal control subjects (n = 29), while patients with Hashimoto's thyroiditis had intermediate values. These results document MnSOD autoantibodies in patients with Graves' disease and suggest that this may result from an immune cross-reactivity between MnSOD and the TSH-receptor.**

PMID: 9633023, UI: 98296679

J Am Coll Nutr 1993 Aug;12(4):384-9

The role of trace minerals in osteoporosis.

Saltman PD, Strause LG

Dept. of Biology, University of California San Diego, La Jolla 92093.

Osteoporosis is a multifactorial disease with dimensions of genetics, endocrine function, exercise and nutritional considerations. **Of particular considerations are calcium (Ca) status, Vitamin D, fluoride, magnesium and other trace elements. Several trace elements, particularly copper (Cu), manganese (Mn) and zinc (Zn), are essential in bone metabolism as cofactors for specific enzymes.** Our investigations regarding the role of Cu, Mn and Zn in bone metabolism include data from studies with animals on Cu- and Mn-deficient diets. We have also demonstrated cellular deficiencies using bone powder implants, as well as fundamental changes in organic matrix constituents. **In clinical studies we have demonstrated the efficacy of Ca, Cu, Mn and Zn supplementation on spinal bone mineral density in postmenopausal women.** Each of these studies demonstrated the necessity of trace elements for optimal bone matrix development and bone density sustenance.

PMID: 8409100, UI: 94013998

In the following study manganese is shown to be an effective inhibitor of bone loss in ovariectomized animals. This indicates that post-menopausal women need adequate manganese to prevent osteoporosis.

Eur J Obstet Gynecol Reprod Biol 2000 May 1;90(1):97-101

Effects on bone loss of manganese alone or with copper supplement in ovariectomized rats. A morphometric and densitometric study.

Rico H, Gomez-Raso N, Revilla M, Hernandez ER, Seco C, Paez E, Crespo E

Departamento de Medicina, Universidad de Alcalá de Henares, 28801, Madrid, Spain

[Record supplied by publisher]

Objective: The aim of this study was to examine the effect of manganese (Mn) alone and with the addition of copper (Cu) in the inhibition of osteopenia induced by ovariectomy (OVX) in rats. Study conditions: Four lots of 100-day-old female Wistar rats were divided into experimental groups of 15 each. One group received a diet supplemented with 40 mg/kg of Mn per kilogram of feed (OVX+Mn). The second group received the same diet as the first, but with an additional 15 mg/kg of copper (OVX+Mn+Cu). The third group of 15 OVX and the fourth group of 15 Sham-OVX received no supplements. At the conclusion of the 30-day experiment, the rats were slaughtered and their femurs and fifth lumbar vertebrae were dissected. Femoral and vertebral length were measured with caliper and bones were weighed on a precision balance. The bone mineral content (BMC) and bone density (BMD) of the femur (F-BMC, mg and F-BMD, mg/cm(2)) and the fifth lumbar vertebra (V-BMC, mg and V-BMD, mg/cm(2)) were measured separately with dual energy X-ray absorptiometry. Results: The F-BMD, mg/cm(2) was lower in the OVX than in the Sham-OVX group (P<0.0001) and in the other two groups receiving mineral supplements (P<0.005 in both). F-BMC, mg was significantly lower in the OVX group than in the other three (P<0.0001 in all cases). Calculations for V-BMC, mg and V-BMD, mg/cm(2) are similar to findings in the femur.

Conclusions: These data show that a Mn supplement is an effective inhibitor of loss of bone mass after OVX, both on the axial and the peripheral levels, although this effect is not enhanced with the addition of Cu.

The following study indicates that manganese blocks the action of calcium ions. This may mean that excessive levels of manganese might interfere with calcium metabolism, requiring a person to need to supplement with more calcium and magnesium.

[Actions of manganese and lanthanum on smooth muscles].

[Article in Japanese]

Sunano S

Effects of Mn^{2+} and La^{3+} on the excitation, contraction, ion movement, and biochemistry of smooth muscles were reviewed. Both Mn^{2+} and La^{3+} block the action potential of smooth muscles without affecting membrane resting potential. However, depolarization or hyperpolarization by these ions and slow discharges which are not affected by these ions have also been reported in some smooth muscles. Mn^{2+} and La^{3+} inhibit the spontaneous contraction and high-K-induced contracture, although these ions can also initiate slow tension development in some preparations. The drug-induced contractions are relatively insensitive to these ions. Mn^{2+} blocks Ca influx, and La^{3+} blocks both Ca influx and efflux. However, La-resistant Ca movements such as Na-Ca exchange or active Ca extrusion have also been reported. La^{3+} also shows effects on the movement of other ions. In biochemical experiments, La^{3+} shows effects on Ca movement of the membraneous and microsomal fractions of smooth muscles, with variations among the smooth muscles. Thus, we should be careful of using these ions as mere Ca blockers.

The following study shows that manganese exposure on a low protein diet will result in a significant increase in dopamine and norepinephrine levels. Norepinephrine is one of the catecholamine stress hormones and high levels can induce hypertension. I wish that the authors had looked at chromium levels. A low protein diet usually means a high carbohydrate diet which will deplete chromium. Since chromium is an antagonist of manganese, it is possible that the effect is not due per se to low protein but to a combination of high manganese with low chromium.

Neurobehav Toxicol Teratol 1985 Sep-Oct;7(5):427-31

Effect of low protein diet on manganese neurotoxicity: III. Brain neurotransmitter levels.

Ali MM, Murthy RC, Mandal SK, Chandra SV

The effect of concurrent low protein (10% casein) diet and manganese (Mn) exposure (3 mg/ml drinking water) on brain levels of dopamine (DA), norepinephrine (NE) and 5-hydroxytryptamine (5-HT) were investigated in Fo-growing (90 days exposure), Fo-diet rehabilitated (low----normal protein diet-28 days) and F1-weaned rats. Mn exposure in either diet group resulted in a significant increase in the DA and NE levels but a decrease in the 5-HT level. These effects were more pronounced in the rats fed the low protein diet, especially in the F1-offsprings. Diet rehabilitation reduced the effects of Mn exposure.

Title

Heavy metal concentrations in blood cells in patients with amyotrophic lateral sclerosis.

Author

Nagata H; Miyata S; Nakamura S; Kameyama M; Katsui Y

Source

J Neurol Sci, 67(2):173-8 1985 Feb

Abstract

Manganese (Mn) and selenium (Se) concentrations in blood cells were measured by neutron activation analysis. Blood was obtained from patients with **amyotrophic lateral sclerosis (ALS)**, patients with other neurological diseases and control subjects. Dried blood cells were activated by neutron irradiation. Mn was determined after chemical separation and Se was determined nondestructively. **Mn concentrations in blood cells from ALS patients were significantly lower (P less than 0.01) than those from the other groups.** The Mn concentrations were also significantly lower (P less than 0.01) in late than in earlier stages of ALS. Se concentrations in blood cells from ALS patients were significantly higher (P less than 0.01) than those from the other two groups. A generalized abnormal distribution of these metals may play a role in the pathogenesis of this disorder. Bromine, zinc, rubidium, and iron concentrations of erythrocytes were the same in all groups.

Title

Origin of the background sodium current and effects of sodium removal in cultured embryonic cardiac cells.

Author

Mead RH; Clusin WT

Source

Circ Res, 55(1):67-77 1984 Jul

Abstract

Cardiac automaticity is partly due to a diastolic sodium current. Possible mediators of this include tetrodotoxin-sensitive "fast channels, **cesium**-sensitive time-dependent pacemaker current channels, calcium-gated nonspecific channels, and electrogenic sodium-calcium exchange. We have studied the effects of abrupt sodium removal on membrane current and conductance in voltage-clamped chick embryonic myocardial cell aggregates, in the presence of various sodium flux inhibitors. Total replacement of sodium by lithium, Tris, or tetraethylammonium ions in aggregates clamped in the pacemaker range caused a brief outward current followed by a sustained net inward current. The outward current reached a peak value of 1.1 ± 0.5 microA/cm² at a mean latency of 5.4 ± 1.2 sec. ($n = 6$; $V = -70.5 \pm 8.9$ mV; Tris). Conductance often decreased during the outward current. The inward current developed exponentially ($t = 19 \pm 5$ sec) and reached a steady state value of -1.6 ± 0.4 microA/cm². This current was reversed by depolarization (mean reversal potential = -13 ± 13 mV), and was accompanied by increased conductance and spontaneous mechanical activity. Neither of the sodium-removal currents was affected by 20 microM tetrodotoxin. **Cesium** (up to 20 mM) had no effect on the late inward current or the mechanical activity, but decreased the early outward current by $80 \pm 12\%$. **Manganese (25 mM), which blocks sodium-calcium exchange, abolished the late inward current and the mechanical activity. Manganese also reduced the early outward current by $27 \pm 10\%$. Manganese and cesium together blocked all the effects of sodium removal.** We conclude that removal of extracellular sodium interrupts a **cesium**-sensitive "background current, that may be related to the time-dependent pacemaker current, If. Sodium removal also causes gradual activation of a nonspecific conductance, which can ultimately depolarize the cells, and which may be gated by cytoplasmic calcium.

Induction of manganese superoxide dismutase by thyroid stimulating hormone in rat thyroid cells.

Nishida S, Nakano T, Kimoto S, Kusunoki T, Suzuki K, Taniguchi N, Murata K, Tomura TT

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Alterations in the superoxide dismutase (SOD) content of thyroid tissues occurring in association with thyroid dysfunction have been reported. In this study, the Mn-SOD content was found to increase in thyroid tissues of rats administered thyroid stimulating hormone (TSH) and in thyrocytes cultured in medium supplemented with TSH. Furthermore, in the thyroid glands of rats whose serum TSH level was elevated by inhibiting the synthesis of T3 and T4 by 6-methyl-2-thiouracil, the Mn-SOD increased as the TSH concentration increased. In the cultured thyrocytes, the increase in Mn-SOD induced by TSH was inhibited by the C-kinase inhibitor H7. These findings suggest the induction of Mn-SOD by TSH in thyroid cells and point to a role of C-kinase in this process, thereby indicating that a close relationship exists between the serum TSH level and the change in Mn-SOD content in thyrocytes with thyroid dysfunction.

Acta Endocrinol (Copenh) 1993 Dec;129(6):573-8

[t](#)

Localization of Cu/Zn and Mn superoxide dismutase in various thyroid disorders.

Iwase K, Nagasaka A, Kato K, Ohtani S, Tsujimura T, Inagaki A, Jimbo S, Nakai A, Masunaga R, Hamada M, et al

Department of Surgery, Fujita Health University School of Medicine, Toyoake, Japan.

The intracellular localization of Cu/Zn- and Mn-superoxide dismutase (SOD), which catalyze the dismutation of superoxide radicals (O₂⁻) to O₂ and H₂O₂, was studied in the thyroid tissue of various thyroid disorders by an immunohistochemical technique. The concentrations of both SODs in those tissues were measured also by a sandwich enzyme immunoassay technique. Copper/zinc-SOD in thyroid tissues were identified by immunocytochemical staining in most cases of papillary carcinoma and in some cases of other thyroid disorders. In normal follicular cells this enzyme is localized in the perinuclear cytoplasm, whereas in thyroid tumor or hyperplastic follicular cells it exists homogeneously in cytoplasm. **Manganese-SOD stained strongly in papillary carcinoma and papillary-growing cells in the thyroid tissue of adenoma and Graves' disease.** The concentrations of Cu/Zn- and Mn-SOD in thyroid tumor tissues and hyperplastic follicular disorders were significantly higher than those in normal thyroid tissue when they were compared as a function of protein or deoxyribonucleic acid contents. The ratio of Mn-SOD to Cu/Zn-SOD was significantly higher only in papillary carcinoma, except for other thyroid disorders as compared with that in the normal thyroid. In conclusion, SOD seems to be related to cell proliferation and differentiation in the thyroid follicular cell because Cu/Zn-SOD changes its localization in tumor and hyperplastic follicular cells and because the Mn-SOD concentration is increased in papillary carcinoma or papillary-growing cells.

J Toxicol Clin Toxicol 1999;37(2):293-307

Manganese.

Barceloux DG

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Manganese is a very hard, brittle metal, which is used to increase the strength of steel alloys. Absorption from the gastrointestinal tract occurs in the divalent and tetravalent forms. Permanganates, which are strong oxidizing agents, have a +7 valence. The principal organomanganese compound is the anti-knock additive, methylcyclopentadienyl manganese tricarbonyl. Manganese is a ubiquitous constituent of the environment comprising about 0.1% of the earth's crust. For the general population, food is the most important source of manganese with daily intake ranging from 2-9 mg Mn. Combustion of gasoline containing methylcyclopentadienyl manganese tricarbonyl releases submicron particles of Mn₃O₄ that are potentially respirable. Biomagnification of manganese in the food chain probably does not occur. The lungs and gastrointestinal tract absorb some manganese, but the relative amounts absorbed from each site are not known. Homeostatic mechanisms limit the absorption of manganese from the gastrointestinal tract. Elimination of manganese occurs primarily by excretion into the bile. Animal studies indicate that manganese is an essential co-factor for enzymes, such as hexokinase, superoxide dismutase, and xanthine oxidase. However, no case of manganese deficiency in humans has been identified. Manganism is a central nervous system disease first described in the 1800s following exposure to high concentrations of manganese oxides. Manganese madness was the term used to describe the initial psychiatric syndrome (compulsive behavior, emotional lability, hallucinations). More commonly, these workers developed a Parkinson's-like syndrome. Currently, the risks of exposure to low concentrations of manganese in the industrial and in the environmental settings (e.g., methylcyclopentadienyl manganese tricarbonyl in gasoline) are being evaluated with regards to the development of subclinical neuropsychological changes. The American Conference of Governmental and Industrial Hygienists recently lowered the TLV-TWA for manganese compounds and inorganic manganese compounds to 0.2 mg Mn/m³.

Subj: MANGANESE AND NOREPI
Date: 10/19/00 6:31:04 PM Pacific Standard Time
From: BU 007
To: BU 007

Subj: Re: Rigidity
Date: 10/19/00 8:05:33 AM Pacific Daylight Time
From: docv@COX-INTERNET.COM (kirk vestal)
Sender: WILSONS-LIST@LISTSERV.ACSU.BUFFALO.EDU (Wilson's Disease Discussion Group)

Reply-to: WILSONS-LIST@LISTSERV.ACSU.BUFFALO.EDU (Wilson's Disease Discussion Group)
To: WILSONS-LIST@LISTSERV.ACSU.BUFFALO.EDU

mn and mo may be antagonists to cu in someone without wilsons disease. they would be lethal if used solely for treatment in someone with wd in about 6 months to a year! mo is required in 3 enzymes. mo inhibits copper containing enzymes and ceruloplasmin which is a carrier of cu normally. wd people need all the normal copper containing enzymes and ceruloplasmin possible to prevent damage like oxidation causing arthritis, kidney damage, liver damage, basal ganglia damage, etc. the trouble in wd is free cu in the blood getting absorbed at various sites causing damage thru mostly oxidation of surrounding molecules and the lack of normal cu containing enzymes like superoxide dismutase which helps stop oxidative damage. manganese, atomic number 25, is different from magnesium, atomic number 12. i cant find where mn may have an antagonistic effect on cu? mn is required for at least 12 or 15 processes. it is essential to all higher forms of life above a bacteria as it is used in ATP production, an energy metabolite. too much mn or chronic mn poisoning has been described. this occurs in miners, foundry workers, welders, drug manufacturers, potters, glass, ceramic, varnish workers, and food additive workers. the symptoms are schizophrenia and parkinsons like! **it is thought mn is required for norepinephrine synthesis and hence, dopamine synthesis.** mn intoxication has also been found in chronic liver failure victims. i got this data from **Tietz textbook of clinical chemistry 1999 edition.** tietz is more authoritative and safer to rely upon than some natural foods book. drv

Compr Psychiatry 1991 May-Jun;32(3):229-37

Abnormalities in hair trace elements as indicators of aberrant behavior.

Gottschalk LA, Rebello T, Buchsbaum MS, Tucker HG, Hodges EL.

Department of Psychiatry and Human Behavior, College of Medicine, University of California, Irvine 92717.

There are long-standing viewpoints that impulsive and violent behavior may stem from brain dysfunction or damage secondary to head injury, disease, or toxic chemical substances. This research has aimed to examine the relationship between potentially toxic metals and aberrant behavior, especially violent activity, through the noninvasive technique of hair analysis for trace elements. In an initial study, phase I, it was not possible to replicate findings of others who reported high levels of lead, cadmium, and copper in violent offenders. However, high levels of manganese were found in prison versus control groups. In phase II, the possibility of artifactual results arising from prison cooking utensils was controlled for by sampling early after incarceration. Phase III was included to substantiate the initial post hoc findings in an additional jail population. In both latter phases, significantly elevated manganese levels were found in the hair of violent versus nonviolent subjects (P less than .0001). A review of the effects of manganese at deficient and toxic levels does not provide a simple answer as to why manganese levels are elevated in the hair of individuals who have been incarcerated for violent behavior. Our study does not implicate the prison environment or soaps and shampoos used in California prisons. Other factors, such as alcohol, dietary, or psychosocial factors, might influence manganese levels in hair, or any of these factors might function in combination with mild manganese toxicity to contribute to aberrant behavior.

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MONOAMINE OXIDASE (MAO) AND MONOAMINE OXIDASE INHIBITORS (MAOIs).

In the following study, persons with hyperthyroidism were found to have low levels of MAO and DAO (histaminase), both of which are copper-containing enzymes. This is excellent evidence that a copper deficiency is a key part of hyperthyroidism.

Title

Biogenic amines and thyrotoxicosis.

Author

Upadhyaya I; Agrawal JK; Dubey GP; Udupa KN

Address

Centre of Experimental Medicine and Surgery, Banaras Hindu University, Varanasi, India.

Source

Acta Endocrinol (Copenh), 126(4):315-8 1992 Apr

Abstract

Circulating levels of T3, T4, gamma-amino-butyric acid, glutamate, 5-hydroxytryptamine, *histamine*, monoamine oxidase and histaminase were studied in 45 (25M, 20F) hyperthyroid patients and 46 (25M, 21F) normal healthy volunteers. Increased levels of blood 5-hydroxytryptamine, *histamine* and glutamic acid were observed along with elevated T3 and T4, whereas plasma gamma-aminobutyric acid, **monoamine oxidase and histaminase activities were found to be low in both male and female patients.** After three months of treatment, circulating levels of 5-hydroxytryptamine, *histamine* and glutamic acid decreased significantly along with normalization of thyroid hormones and with an increase in the concentrations of gamma-aminobutyric acid, monoamine oxidase and histaminase. There was a positive correlation between these amines and thyroid hormone levels. The findings thus suggest that alterations in the metabolism of biogenic amines may be related to an altered metabolism in thyrotoxicosis, and these parameters may prove to be useful markers for diagnosis and follow-up of these patients.

In the following study monoamine oxidase (type B) and diamine oxidase were found to be low in psoriasis patients while histamine was found to be high. Diamine oxidase is a copper-containing enzyme which breaks down histamine. Histamine is also responsible for asthma which is the reason antihistamines are recommended for asthma. Asthma is probably another disease of copper deficiency.

Title

Monoamine- and diamine oxidase activities in *psoriasis*.

Author

Ionescu G; Kiehl R

Address

Research Department, Spezialklinik Neukirchen, West Germany.

Source

Acta Derm Venereol, 69(3):264-5 1989

Abstract

Monoamine- and diamine oxidase activities were measured by a sensitive photometric assay in 25 *psoriasis vulgaris* patients. Results were compared with plasma histamine values determined fluorimetrically. **Increased plasma histamine levels were associated with significantly lowered diamine--and type B monoamine oxidase activities in platelet-rich plasma of the psoriasis patients.** Our data suggest that cofactor levels and/or inhibiting factors are responsible for the observed monoamine- and diamine oxidase activities.

The following study suggests that licorice has a strong depletion effect on monoamine oxidase. If this is true the consumption of licorice could lead to a worsening of hyperthyroidism (and possibly benefit hypothyroidism).

Author

Hatano T; Fukuda T; Liu YZ; Noro T; Okuda T

Address

Faculty of Pharmaceutical Sciences, Okayama University, Japan.

Source

Yakugaku Zasshi, 111(6):311-21 1991 Jun

Abstract

The roots and/or rhizomes of *Glycyrrhiza uralensis*, *G. glabra* and *G. inflata*, and commercial *licorice* specimens from various regions or countries were analyzed by high-performance liquid chromatography (HPLC), and classified into three types based on their phenolic constituents. i) Type A: The roots and rhizomes of *G. uralensis*, commercial *licorice* specimens from northwestern region of China (Seihoku-kanzo) and from northeastern region of China (Tohoku-kanzo) in Japanese markets, and also several licorice specimens from Chinese markets. They contain licochalcone (6), glycycomarin (7) and/or licochalcone (8), which were not found in *G. glabra* and *G. inflata*. ii) Type B: The root and rhizome of *G. glabra*, and the *licorice* specimens imported from the Soviet Union and Afghanistan. They contain glabridin (9) and glabrene (10), which were not found in the samples of the other two *Glycyrrhiza* species. A root sample of *Glycyrrhiza* species from Turkey also contains 9 and 10. iii) Type C: The root sample of *G. inflata*. They contain licochalcones A (11) and B (12), which were not found in the samples of the other two *Glycyrrhiza* species. Commercial *licorice* specimens obtained in Japan, which were imported from Sinkiang of China (Shinkyo-kanzo), and some licorice specimens obtained from Chinese markets, have also been found to contain 11 and 12. The phenolics 6-12, characteristic constituents of types A, B or C, were not found in a specimen of cortex-free *licorice* from a Japanese market (kawasaki-kanzo). Extracts of some *licorice* specimens of types A and B, and all of the *licorice* specimens of type C inhibited 40-56% of the xanthine oxidase activity at the concentration of 30 micrograms/ml. **Extracts of some licorice specimens of types A and B also showed inhibitory effects on monoamine oxidase (44-64% inhibition, at the concentration of 30 micrograms/ml), which were slightly weaker than that of harmaline hydrochloride.**

Title

Monoamine and diamine oxidase activity in the diagnosis of carcinoid tumors.

Author

Feldman JM

Source

Cancer, 56(12):2855-60 1985 Dec 15

Abstract

This study determines if one could distinguish foregut from midgut carcinoid tumors by quantitative measurement of the monoamine oxidase (MAO) and diamine oxidase (DAO) activities in homogenates of tumors. The MAO activity of 16 foregut carcinoid tumors (1850 +/- 342 pmol/mg/minute) was significantly higher than the MAO activity of 11 midgut carcinoid tumors (407 +/- 43 pmol/mg/minute, P less than 0.01) with no overlap between the groups. Although all ten of the midgut carcinoids had measurable DAO activity (720 +/- 190 pmol/mg/minute), with the exception of one duodenal carcinoid tumor (33 pmol/mg/minute) the nine foregut carcinoid tumors evaluated did not have detectable DAO activity. The MAO activity of all of the foregut carcinoids was higher than that of 6 islet cell tumors, 28 paragangliomas, and 12 medullary carcinomas of the thyroid. Quantitative MAO and DAO activity may be useful in distinguishing foregut carcinoid tumors from other related tumors.

Title

Serotonin metabolism and platelet monoamine oxidase activity in patients with medullary carcinoma of the thyroid and pheochromocytoma.

Author

Feldman JM; Farrell RE; Wells SA Jr

Source

Am J Med Sci, 278(1):39-48 1979 Jul-Aug

Abstract

Occasional patients with medullary carcinoma of the thyroid (Multiple Endocrine Neoplasia Type II [MEN II]) are reported to have excessive serotonin (5-HT) production from the MCT; almost all patients with metastatic MCT have elevations in plasma concentration of the amine oxidase, histaminase. The elevated 5-HT production is thought to contribute to the troublesome diarrhea experienced by patients with MEN II. We compared the urinary excretion of 5-hydroxyindoleacetic acid (5-HIAA), the principle metabolite of 5-HT, of 33 patients with MCT with the urinary excretion of 5-HIAA in 33 control subjects. Six of the 33 MCT patients (18%) had severe diarrhea. The 5-HIAA excretion of the MCT patients did not differ from that of normal subjects. We also compared the platelet monoamine oxidase (MAO) activity of 27 MCT patients and 27 control subjects. The platelet MAO activity of the two groups did not differ. The 5-HT content and MAO activity of 6 of the MCTs was similar to normal thyroid tissue. The MAO activity of two follicular adenomas of the thyroid was greater than the MAO activity of MCTs. In contrast to the uniform elevation of plasma histaminase in patients with MCT, the platelet MAO activity is not altered and the majority of MCTs do not produce excessive amounts of 5-HT.

MONOAMINE OXIDASE POST TO GROUP, Jan.14, 1999

When I learned about monoamine oxidase (MAO) I had a feeling that this could be a very big story for hypers and pheos. When I did a Medline search of MAO I found over 1300 scientific studies dealing with it. There is no doubt in my mind now that MAO deficiency is a major cause, and perhaps the biggest cause, of hyperT and phéo.

As I explained before, I am going to reorganize my posts on these studies and give a summary first. This way you can determine if this study is pertinent to you and the layout will conform more to the standard organization of reports on scientific studies.

There are many studies which show that monoamine oxidase (MAO) is a copper-containing enzyme which deactivates the catecholamines (norepinephrine, epinephrine, and dopamine) after their function has ended. There are some studies showing that MAO deficiency increases thyroid hormones. One study showed that a copper deficiency causes a deficiency of MAO. Another study stated that MAO contains iron. Several studies showed that long-term exposure of rats and humans to manganese (a copper and iron antagonist) causes MAO deficiency. Many of the symptoms seen in hyperT and phéo are appear directly attributable to MAO deficiency from copper deficiency. Stress initiates higher production of catecholamines which require more MAO for degradation, and thereby may cause decreased copper levels. These nutrients appear to be necessary for MAO production: copper, iron, riboflavin, histidine, and vitamin C.

The full story is more complex. First there are two isozymes of MAO: MAO-A and MAO-B. Also there are other similar enzymes that degrade hormones and neurotransmitters. (The terms degradation, deamination, and deactivation will be used interchangeably in this story.)

There is a diamine oxidase (DAO) which has two amines instead of the one amine in MAO. There is dopamine beta-hydroxylase (DBH). There is also semicarbazide-sensitive amine oxidase (SSAO) and others. I don't want to make it complicated but just want you to be aware that there is a whole family of oxidases which degrade hormones and neurotransmitters.

MAO is well studied and has been shown to contain topa quinone. Topa is 2,4,5-trihydroxyphenylalanine (built on the amino acid phenylalanine) and copper is essential for its production. MAO contains histidine, another amino acid. I will do another post on histidine in the future. Since histidine is an amino acid found in proteins, I don't think you need to supplement it, but it is available as a supplement if you wish to try it.

One study directly showed that a copper deficiency causes a deficiency of MAO. Another study indicated that MAO contains iron. Another study showed that copper and flavin (riboflavin) were necessary for MAO production and that the human heart has high MAO-B activity. This suggests to me that MAO deficiency could cause increased heart rate and therefore a copper and/or iron deficiency can cause increased heart rate. Another study showed that imbalances in body levels of copper and zinc can cause hypertension and that low MAO causes higher blood pressure.

The catecholamines, epinephrine (the other name is adrenalin), norepinephrine (noradrenalin), and dopamine, are the stress hormones which get your body ready for fight-or-flight emergencies. In normal humans (and other mammals), MAO-A and MAO-B deactivate these hormones so that the body can return to a calm state. When the animal is frightened by a primary or

conditioned response stimulus, these hormones are squirted into circulation to increase heart rate, breathing rate, and blood pressure to ready the animal for fighting or running away. If the MAOs are lacking, then these hormones are not degraded and remain in circulation for a long time, causing the prolonged panic and anxiety attacks seen in hyperT and phéo.

Studies show that both MAO-A and MAO-B deaminate norepinephrine, with MAO-A deactivating about 2/3 of the norepi and MAO-B deactivating 1/3. Many people have depression and fatigue caused by insufficient amounts of the stimulating catecholamines (perhaps from insufficient tyrosine or phenylalanine in their diets, or other nutrient deficiencies). Doctors often prescribe monoamine oxidase inhibitors (MAOI) to increase the available amounts of the catecholamines. L-Deprenyl (Selegiline) is a drug which inhibits MAO-B, while Clorgyline inhibits MAO-A. Other MAO inhibitors are ifenprodil and beflaxatone. If you are taking any drugs, find out through the Physicians Desk Reference (PDR) whether those drugs are MAOIs.

Studies have shown that norepi increases during chronic MAO inhibition through the use of an MAOI. So the studies show clearly that norepi and the other catecholamines are decreased by MAO and increase when MAO is deficient.

Several studies on rats have been done to see the effects of MAOs on thyroid hormone. Methimazole (trade name Tapazole) has been shown to increase MAO activity (mainly MAO-A) and thereby increase TSH. Another study showed that MAO inhibitors increase T4, showing that low MAO causes increased thyroid hormone. Another study showed that an MAOI increased wheel running in normal (euthyroid) rats more than hypothyroidic rats, indicating that MAOs affect the thyroid levels. Another study showed that rats treated with thyroxine (T4) had decreased levels of MAO, and those treated with carbimazole (methimazole) had increased levels of MAO.

Quite a few studies have been done on rats showing the effects of manganese on MAO. One study showed that prolonged exposure to low levels of manganese caused MAO to be decreased significantly. Another study showed that manganese given to rats at high levels showed significant reduction in both MAO-A and MAO-B. Another study showed that manganese in rat drinking water decreased dopamine beta-hydroxylase. A study showed manganese-exposed human workers in a ferro-alloy manufacturing plant had lower MAO-B activity. Since manganese is copper and iron antagonist, it appears that the effects of manganese on MAO are mediated by decreasing copper and iron levels.

Studies on manganese and thyroid function are less conclusive but suggestive. One study showed that manganese deficiency increases 5'-deiodinase activity (increased conversion of T4 to T3), while another study showed that excess manganese caused thyroid abnormalities (?). It appears that excess manganese can have significant effects on catecholamine levels (and possibly thyroid levels) by decreasing both MAOs significantly. I think all phéos and hypers need to determine if their manganese levels are high. Since many multiple vitamin/mineral supplements contain 5-10 mg of manganese, the use of these products in phéos and hypers with high body levels of manganese could be very detrimental. Supplementation with copper and iron is very important whether or not manganese levels are high.

One study was performed on the effects of stress on cardiovascular and cerebrovascular disorders (heart and brain circulation). The study showed that high levels of stress cause high levels of epinephrine. The epi is deactivated by MAO to form methylamine which is then converted by SSAO (semicarbazide-sensitive amine oxidase) to formaldehyde, hydrogen peroxide, and ammonia. These chemicals can cause extensive damage to the brain and heart. This appears to be what happens in phéo and untreated hyperT.

Another study showed that SSAO is active in many part of the eye. My speculation is that high levels of catecholamines or thyroid hormones in the eye may cause SSAO to produce excess formaldehyde or other breakdown products which may damage the eye. Since riboflavin is involved in MAO production and also helps prevent many eye problems, there may be some connection.

One study showed that in ulcerative colitis, which is an inflammation of the colon, there is a deficiency of diamine oxidase and MAO which decreases the ability of the bowel to produce the amino acid GABA which then leads to an inflammation of the mucosa. Since hypers (I don't know about phéos) have bowel problems (diarrhea etc.), then there may be some connection here.

Several studies have been done on whether B-12 deficiency affects MAO. One study showed no association. Another showed B-12 status is a controlling factor in platelet MAO activity (I don't know what this is.) Another study showed a negative association between MAO-B activity and B-12 levels. This indicates that when B-12 is administered, MAO-B activity decreases. I have speculated in the past that B-12 shots seem to increase hyperT symptoms. I think that when B-12 is taken without iron it causes the iron to be further depleted.

Literature on copper indicates that high copper levels can lead to schizophrenia by deactivating the catecholamines and serotonin. In other words high levels of copper can increase the MAOs and thereby cause deficiencies of catecholamines and serotonin. Do hypers and phéos have to worry about getting too much copper and becoming schizophrenic? I don't think so. First the copper would have to increase to the point where the MAOs would be high enough to eliminate all symptoms of their disease, and then as copper increased more you would get hypothyroid, and then more copper would lead to severe depression and fatigue. Finally very high levels of copper could lead to schizophrenia. More than likely these high levels of copper cannot be achieved without taking massive doses of copper (over 50 mg a day) and/or not taking the other minerals which work with copper (iron, sulfur, zinc, etc.) Hypers and phéos seem to be on the extreme other end of the spectrum of copper levels from the schizophrenics.

An interesting study showed that there is a Dutch family which has a genetic defect which causes a deficiency of MAO-A (which degrades serotonin and norepi). Norepi increases anger, while serotonin suppresses fear. The men in this family had double the normal levels of norepi and nine times the normal levels of serotonin. The high norepi made them get angry easily and the high serotonin almost completely eliminated any feelings of fear. The result: high aggression and violent behavior. They get angry and have no fear of the consequences of attacking those who make them angry.

People with high fear levels (phobias, anxiety, etc.) are usually deficient in serotonin. The amino acid tryptophan is converted into niacin which is converted into serotonin. Supplementation of tryptophan (you'll need a doctor's prescription) or niacin will increase serotonin production and lower fear levels. Prozac and other similar drugs increase serotonin by decreasing its degradation, enabling the users to live life with less fear. It's easy to do the same thing by increasing tryptophan in the diet or supplementing with more niacin (and safer too.)

In summary, we have known for a long time that copper decreases the symptoms of hyperthyroidism but had only one explanation for the possible action--increasing estrogen production, which suppresses thyroid activity. Now we have what is probably the most important reason why copper helps hypers (and hopefully pheos)--it is essential for production of MAOs which deactivate the catecholamines and the thyroid hormones. Low copper leads to low MAO which leads to hyperT and phoe. Also low levels of the other nutrients known to be involved in MAO production may play a role: iron, histidine, riboflavin, and vitamin C. It is quite likely that other nutrients are essential for MAO production.

Whether MAO can be taken directly to control hyperT and phoe is an interesting question for which I have no answer. If it were possible to obtain MAO, this would be a great experiment which could show us whether MAO deficiency is causing these diseases. I saw no study in which MAO was administered to any human or other animal, so perhaps it doesn't exist.

Because there seem to be many of these oxidases, the best solution seems to be to increase the nutrients needed to produce them. Since these nutrients seem to be the ones that we have been using, then it appears that if MAO deficiency is the cause of these diseases, then we are proceeding in the right direction.

The one new discovery from this in regards to what nutrients may be important in recovery from hyperT and phoe is histidine. Histidine is an amino acid that I suspected was involved a few weeks ago. I have been supplementing with it on and off for a few weeks now and haven't noticed any big effects. But it might have a big effect on anyone who is deficient in it or who has hyperT or phoe. I suspect that a high protein diet will supply an adequate amount of histidine and that the limiting nutrients for most hypers and pheos are copper, iron, and the B-complex vitamins.

I will continue studying the degradation of hormones and feel that right now this seems to be the most promising area of research for hyperT and phoe. I will also try to determine if some hypos have excess MAO and this is the cause of their condition. I suspect that most hypos are deficient in the nutrients needed to make thyroid hormone, some possibly from excess levels of competing nutrients or toxic metals.

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MERCURY

Mercury is a toxic metal with significant effects on the thyroid. There is ample evidence that mercury leaches from dental amalgam fillings and contributes to thyroid disease and anemia.

While large doses of mercury can induce hyperthyroidism, smaller amounts can induce hypothyroidism by interfering with both the production of thyroxin (T4) and the conversion of T4 to T3.

Mercury disturbs the metabolism of copper and zinc which are two minerals critical to thyroid function. Gray hair can be an indication of mercury accumulation, more so in females than males.

Mercury causes disruptions to the immune system functioning and promotes the production of IgG and IgE autoantibodies which also are involved in autoimmune thyroid disease.

Different forms of mercury, organic or inorganic, have different effects on the thyroid. Milk and quite likely estrogen cause an increase in the absorption of mercury.

Mercury has a very long half-life in the body with a duration of perhaps many years and has been found in cancerous tissues.

Selenium is the key mineral which protects the body from mercury toxicity. One study showed that cilantro (Chinese parsley) helps remove mercury from the body and protects the body from pre-cancerous lesions.

As the following article indicates mercury gets into our bodies in a variety of ways including vaccinations. Perhaps the negative effects we see from vaccines are at least partially the result of toxic metals. The association of autism with vaccinations may be related to mercury toxicity. Thimerosal is the mercury-containing preservative that was used in contact lens solutions. Hopefully there are no more of these solutions on the market but if you use contact lens solutions, check the label.

US Congressman Dan Burton Requests Immediate Vaccine Recall

In an October 25, 2000 letter to [Department of Health and Human Services \(HHS\)](#) Secretary Donna Shalala, Congressman Dan Burton (R-IN), Chairman of the House Committee on Government Reform, requested a recall of all vaccines containing Thimerosal. The mercury-based product Thimerosal is added to vaccines as a preservative.

On July 18, 2000 the Committee conducted a hearing entitled, "Mercury in Medicine: Are We Taking Unnecessary Risks?" During the hearing, **the FDA admitted that children are being exposed to unsafe levels of mercury through vaccines containing Thimerosal.** It was also determined that symptoms of mercury poisoning mimic symptoms of autism -- a disease that has reached epidemic levels in the United States. However, the FDA has chosen to allow pharmaceutical companies to merely phase out their use of Thimerosal, leaving mercury-containing vaccines at public and private health facilities.

In his letter to Secretary Shalala, Chairman Burton stated:

"We all know and accept that mercury is a neurotoxin, and yet the FDA has failed to recall the 50 vaccines that contain Thimerosal...On their own website, the FDA states, 'lead, cadmium, and mercury are examples of elements that are toxic when present at relatively low levels'..."

"Our children are the future of this country. As a Government we have a responsibility to do everything within our power to protect them from harm, including ensuring that vaccines are safe and effective. Every day that mercury-containing vaccines remain on the market is another day HHS is putting 8,000 children at risk. Given that Thimerosal-free vaccines are available, and the known risk of mercury toxicity, to leave Thimerosal-containing vaccines on the market is unconscionable."

Title

Thyrotoxicity of the chlorides of cadmium and mercury in rabbit.

Author

Ghosh N; Bhattacharya S

Address

Department of Zoology, Visva-Bharati University, Santiniketan, India.

Source

Biomed Environ Sci, 5(3):236-40 1992 Sep

Abstract

Exposure to heavy metals such as cadmium and mercury is of immediate environmental concern. The present study was aimed at establishing a direct relationship between heavy metal poisoning and thyroid dysfunction. **Cadmium and mercury treatment at LD50 levels resulted in severe thyrotoxicosis in the rabbit.** Within 24 h of intramuscular administration of cadmium chloride 15 mg.kg⁻¹ body weight (bw) and mercury chloride 20 mg.kg⁻¹ bw, thyroid peroxidase activity increased significantly over the control with a concomitant rise in the triiodothyronine (T3) titre. On the other hand, there was a remarkable fall in the thyroxine (T4) level, and the T3/T4 ratio was high as compared with the control. **Evidence indicates that acute heavy metal lethality will induce immediate hyperthyroidism.** It is suggested that T3-toxicosis may be produced by a preferential synthesis of T3 and/or preferential deiodination of T4 to T3. Measurement of T3 and T4 levels may thus be utilized as a reliable indicator of heavy metal lethality.

The following study showed that the administration of mercury in the form of mercuric chloride causes significant alterations in copper and zinc metabolism, but does not seem to affect iron metabolism. While the thyroid functions were not examined in this study, the fact that mercury has such profound effects on copper and zinc metabolism suggests that thyroidal function will be disturbed by mercury.

Title

Effect of acute administration of mercuric chloride on the disposition of copper, *zinc*, and iron in the rat.

Author

Huang YL; Lin TH

Address

School of Technology for Medical Sciences, Kaohsiung Medical College, Taiwan, ROC.

Source

Biol Trace Elem Res, 58(1-2):159-68 1997 Jul-Aug

Abstract

The present study was designed to investigate the effect of mercuric chloride administration on copper, *zinc*, and iron concentrations in the liver, kidney, lung, heart, spleen, and muscle of rats. The results showed that after dose and time exposure to mercuric chloride, the concentration of mercury in the six tissues was significantly elevated. **Data showed that there were no interaction between mercury and tissue iron. There was a considerable elevation of the content of copper in the kidney and liver. The most significant changes in the copper concentration took place in the kidneys. About a twofold increase in the copper content of the kidney was noted after exposure to mercuric chloride (3 mg and 5 mg/kg).** Only slight elevations in the copper content occurred in the liver especially in high dose and longer exposure time. In the remaining organs, the copper content was not changed significantly ($p > 0.05$). **The most significant changes in the zinc concentration took place in liver, kidney, lung and heart (5 mg/kg).** Marked changes in kidney *zinc* concentrations were observed at any of the specified doses. *Zinc* concentrations were significantly increased in kidney of rats sacrificed 9-48 h after s.c. injection of HgCl₂ (5 mg/kg); in liver obtained from rats at 18, 24 or 48 h after injection; and in lung after 24 or 48 h of treatment. The heart and spleen *zinc* concentrations were elevated at 24 and 48 h after injection of HgCl₂ (5 mg/kg), respectively. **The results of this study implicate that effects on copper and zinc concentrations of the target tissues of mercury may play an important role in the pathogenesis of acute mercuric chloride intoxication.**

The following study suggests that mercury content in females can be judged by hair color. Gray hair contains more organic mercury than dark hair in both sexes, but there is a sex difference in that mercury seems to more readily turn hair gray in females than in males.

Title: Mercury concentration in gray hair

Author: Ando T; Wakisaka I; Yanagihashi T; Tomari T; Hatano H

Source: Nippon Eiseigaku Zasshi, 43(6):1063-8 1989 Feb

Abstract

Scalp hair sample were collected from 20 gray-haired males and 7 gray-haired females. Two hair samples, one each of dark hair and gray hair, obtained from each individual were selectively analysed for organic and inorganic *mercury* concentrations. The following finding were made: 1) In both sexes, total and organic *mercury* concentrations were significantly higher in gray hair than in dark hair but no difference was observed between dark hair and gray hair for the concentration of inorganic *mercury*. 2) For males, no significant differences between dark hair and gray hair were found for total, organic or inorganic *mercury* concentrations. On the other hand, gray hair had significantly higher levels of total, organic and inorganic *mercury* concentrations than dark hair in females. 3) When comparison was made between the sexes, total, organic and inorganic *mercury* concentrations were significantly higher in males than in females for dark hair. For gray hair, however, significantly higher levels of total and organic *mercury* concentrations, but not of inorganic *mercury* concentrations, were found in males. 4) The proportion of inorganic *mercury* to total *mercury* was higher in females than in males for both dark and gray hair. It was also higher in gray hair than in dark hair for females.

The following study explores the detoxifying effect that selenium has on mercury. Apparently one atom of selenium combines with one atom of mercury to form a biologically inactive complex.

Title

Mercury/selenium interaction. A comparative study on pigs.

Author

Hansen JC; Kristensen P; Al-Masri SN

Source

Nord Vet Med, 33(2):57-64 1981 Feb

Abstract

A pilot experiment carried out on three pigs have confirmed that interaction between inorganic *mercury* (203HgCl₂) and selenium (Na₂75SeO₃) after single intraperitoneal injections are qualitatively uniform in mice and pigs. **The detoxifying effect of selenium on mercury toxicity seems to be due to a formation of a biologically inactive complex containing the elements in an equimolar ratio.** The

complex is unable to pass biological barriers, placenta and choroid plexus and is stored in the liver and the spleen.

The following study explores the interaction between mercury and selenium when administered at different times. The greatest cancellation of effects occurred when both were administered simultaneously.

Title

Effect of administration sequence of mercuric chloride and sodium selenite on their fates and toxicities in mice.

Author

Naganuma A; Ishii Y; Imura N

Source

Ecotoxicol Environ Saf, 8(6):572-80 1984 Dec

Abstract

Interaction of *mercury* and selenium was examined in mice given mercuric chloride (25 $\mu\text{mol/kg}$) intravenously with sodium selenite (25 $\mu\text{mol/kg}$, iv) according to various administration schedules. Body weight of the mice given mercuric chloride or selenite alone did not increase, but the mice given both compounds simultaneously grew as well as control mice. On the other hand, only a 1-hr shift of administration of either compound canceled the mutual detoxifying effect. The most conspicuous changes in tissue distribution of *mercury* and selenium and in gel filtration patterns of both elements accumulating in tissues of the mice were observed when both compounds were administered simultaneously. **These experimental results indicate that the interaction of mercuric mercury with selenite in mice occurred to the greatest extent upon simultaneous administration, supporting the hypothesis that the interaction primarily occurs in the blood stream.**

The following study analyzed mercury and selenium concentrations in cadavers of workers in dental offices and found that there were increased concentrations of selenium and mercury showing that selenium accumulated together with mercury.

Br J Ind Med 1991 Nov;48(11):729-34

Mercury and selenium concentrations and their interrelations in organs from dental staff and the general population.

Nylander M, Weiner J

Department of Environmental Hygiene, Karolinska Institute, Stockholm, Sweden.

Mercury (Hg) and selenium (Se) concentrations were determined by radiochemical neutron activation analysis in samples from the pituitary glands, occipital cortices, renal cortices, abdominal muscles, and thyroid glands of cadavers. Samples were retrieved from dental staff occupationally exposed to Hg and from the general population. **Increased concentrations of both Hg and Se in samples from dental staff showed that Se accumulated together with Hg.** Regression analysis of data from the pituitary glands and occipital cortices of dental staff indicated the accumulation of Se at a rough stoichiometric ratio of 1:1 with Hg. The same stoichiometric ratio between the elements was seen in the renal cortices from the general population. The regression analysis showed that a substantial fraction of Se was not associated with Hg; it is assumed that this corresponds to biologically available Se. Concentrations of biologically available Se decreased with advancing age in the pituitary gland, but not in other organs, and varied appreciably between organs.

The results of the following study "suggest that mercury poisoning from dental amalgam may play a role in the etiology of cardiovascular disorders." "Hemoglobin, hematocrit, and red blood cells were significantly lower when correlated to increased levels of urine mercury. The amalgam subjects had a greater incidence of chest pains, tachycardia, anemia, fatigue, tiring easily, and being tired in the morning." This indicates that mercury toxicity can induce anemia and all the symptoms of anemia. We have seen elsewhere that there is a high association of anemia with thyroid disorders. Mercury toxicity from dental amalgam would seem to be a prime contributor to anemia and thyroid disease.

: *Sci Total Environ* 1990 Dec 1;99(1-2):23-35

The relationship between mercury from dental amalgam and the cardiovascular system.

Siblerud RL

Department of Physiology, College of Veterinary Medicine and Biological Sciences, Colorado State University, Fort Collins 80523.

The findings presented here suggest that mercury poisoning from dental amalgam may play a role in the etiology of cardiovascular disorders. Comparisons between subjects with and without amalgam showed amalgam-bearing subjects had significantly higher blood pressure, lower heart rate, lower hemoglobin, and lower hematocrit. **Hemoglobin, hematocrit, and red blood cells were significantly lower when correlated to increased levels of urine mercury. The amalgam subjects had a greater incidence of chest pains, tachycardia, anemia, fatigue, tiring easily, and being tired in the morning.** The data suggest that inorganic mercury poisoning from dental amalgam does affect the cardiovascular system.

PMID: 2270468, UI: 91102526

The following study shows that mercury accumulates in various structures of the eye and that the half-life of mercury in the body probably exceeds years.

Title

***Mercury* accumulation in the squirrel monkey eye after *mercury* vapour exposure.**

Author

Warfvinge K; Bruun A

Address

Source

Toxicology, 107(3):189-200 1996 Mar 18

Abstract

Squirrel monkeys were exposed to *mercury* vapour at different concentrations and for different numbers of days. The calculated total *mercury* absorption ranged between 1.4-2.9 mg (range of daily absorption 0.02-0.04 mg). The monkeys were killed at different intervals after the end of exposure (range 1 month - 3 years) and the eyes were enucleated. Eyes from four un-exposed monkeys were used as control material.

Mapping of the mercury distribution in the eye revealed that the non-myelin-containing portion of the optic disc was densely loaded with mercury deposits, which are mostly confined to the capillary walls and the glial columns. The white matter of the brain does not accumulate *mercury* at these exposure levels, which might suggest that the myelinization process inhibits the accumulation of *mercury*. The pigmented epithelium of the pars plicata of the ciliary body and of the retina contained a considerable amount of *mercury*. This finding indicates that *mercury* is trapped within the melanocytes, which keeps potentially dangerous material from reaching the neural retina. **In addition, the retinal capillary walls were densely loaded with mercury deposits, even 3 years after exposure.** It was also found that the inner layers of the retina accumulated *mercury* during a 3-year period. **It is known that the biological half-time of mercury in the brain may exceed years. This seems also to be the case for the ocular tissue.**

The following study is a strong indictment of the use of mercury in dental materials. Not only is it stated that mercury causes a reduced effectiveness against bacteria such as Chlamydia, Streptococcus, and Borrelia, and Herpes family viruses, but mercury has been found in pre-cancerous and cancerous tissues. Of particular interest was the authors' discovery that cilantro (Chinese parsley) is effective in removing mercury from the body and in reversing pre-cancerous abnormalities.

Acupunct Electrother Res 1996 Apr-Jun;21(2):133-60

Significant mercury deposits in internal organs following the removal of dental amalgam, & development of pre-cancer on the gingiva and the sides of the tongue and their represented organs as a result of inadvertent exposure to strong curing light (used to solidify synthetic dental filling material) & effective treatment: a clinical case report, along with organ representation areas for each tooth.

Omura Y, Shimotsuura Y, Fukuoka A, Fukuoka H, Nomoto T

Heart Disease Research Foundation, New York, USA.

Because of the reduced effectiveness of antibiotics against bacteria (e.g. Chlamydia trachomatis, alpha-Streptococcus, Borrelia burgdorferi, etc.) and viruses (e.g. Herpes Family Viruses) in the presence of mercury, as well as the fact that the 1st author has found that mercury exists in cancer and pre-cancer cell nuclei, the presence of dental amalgam (which contains about 50% mercury) in the human mouth is considered to be a potential hazard for the individual's health. In order to solve this problem, 3 amalgam fillings were removed from the teeth of the subject of this case study. In order to fill the newly created empty spaces in the teeth where the amalgams had formerly existed, a synthetic dental-filling substance was introduced and to solidify the synthetic substance, curing light (wavelength range reportedly between 400-520 nm) was radiated onto the substance in order to accelerate the solidifying process by photo-polymerization. In spite of considerable care not to inhale mercury vapor or swallow minute particles of dental amalgam during the process of removing it by drilling, mercury entered the body of the subject. Precautions such as the use of a rubber dam and strong air suction, as well as frequent water suctioning and washing of the mouth were insufficient. Significant deposits of mercury, previously non-existent, were found in the lungs, kidneys, endocrine organs, liver, and heart with abnormal low-voltage ECGs (similar to those recorded 1-3 weeks after i.v. injection of radioisotope Thallium-201 for Cardiac SPECT) in all the limb leads and V1 (but almost normal ECGs in the precordial leads V2-V6) the day after the procedures were performed. Enhanced mercury evaporation by increased temperature and microscopic amalgam particles created by drilling may have contributed to mercury entering the lungs and G.I. system and then the blood circulation, creating abnormal deposits of mercury in the organs named above. Such mercury contamination may then contribute to intractable infections or pre-cancer. **However, these mercury deposits, which commonly occur in such cases, were successfully eliminated by the oral intake of 100 mg tablet of Chinese parsley (Cilantro) 4 times a day (for average weight adults)** with a number of drug-uptake enhancement methods developed by the 1st author, including different stimulation methods on the accurate organ representation areas of the hands (which have been mapped using the Bi-Digital O-Ring Test), without injections of chelating agents. Ingestion of Chinese parsley, accompanied by drug-uptake enhancement methods, was initiated before the amalgam removal procedure and continued for about 2 to 3 weeks afterwards, and ECGs became almost normal. During the use of strong bluish curing light to create a photo-polymerization reaction to solidify the synthetic filling material, the adjacent gingiva and the side of the tongue were inadvertently exposed. This exposure to the strong bluish light was found to produce pre-cancerous conditions in the gingiva, the exposed areas of the tongue, as well as in the corresponding organs represented on those areas of the tongue, and abnormally increased enzyme levels in the liver. **These abnormalities were also successfully reversed by the oral intake of a mixture of EPA with DHA and Chinese parsley,** augmented by one of the non-invasive drug-uptake enhancement methods previously described by the 1st author, repeated 4 times each day for 2 weeks.

The following study demonstrates that in genetically susceptible species (and this may include many humans), mercury leaches from dental amalgam fillings and causes a rapid activation of the immune system. Up to a 12-fold increase in IgE concentrations were found within 3 weeks. The mercury was also found to cause large tissue increases in silver, copper, and selenium, which are three minerals that I suspect are important in the control of the immune response. Selenium has been demonstrated to be an important detoxifier of mercury and I suspect that copper and silver are also involved in the mitigation of the toxic effects of mercury.

Title

Activation of the immune system and systemic immune-complex deposits in Brown Norway rats with dental amalgam restorations.

Author

Hultman P; Lindh U; H"orsted-Bindslev P

Address

Department of Health and Environment, Link"oping University, Sweden.

Source

Abstract

Dental amalgam restorations are a significant source of mercury exposure in the human population, but their potential to cause systemic health effects is highly disputed. We examined effects on the immune system by giving genetically mercury-susceptible Brown Norway (BN) rats and mercury-resistant Lewis (LE) rats silver amalgam restorations in 4 molars of the upper jaw, causing a body burden similar to that described in human amalgam-bearers (from 250 to 375 mg amalgam/kg body weight). BN rats with amalgam restorations, compared with control rats given composite resinous restorations, developed a rapid activation of the immune system, with a maximum 12-fold increase of the plasma IgE concentration after 3 wks ($p < 0.001$; Mann-Whitney's test). LE rats receiving amalgam restorations showed no significant increase of plasma IgE ($p > 0.05$). After 12 wks, BN rats with amalgam restorations showed significantly increased ($p < 0.05$) titers of immune-complex (IC) deposits in the renal glomeruli and in the vessel walls of internal organs. These rats also showed a significant ($p < 0.05$), from six- to 130-fold, increase in tissue mercury concentration in the concentration order kidney > spleen > cerebellum occipital lobe > cerebellum > liver > thymus, and the tissue silver concentration was significantly ($p < 0.05$) increased from three- to 11-fold. Amalgam-implanted BN rats showed a significant ($p < 0.05$) increase in copper concentration in the kidney and spleen, and in kidney selenium concentration. We conclude that dental amalgam restorations release substantial amounts of their elements, which accumulate in the organs and which, in genetically susceptible rats, give rise to activation of the immune system and systemic IC deposits.

The following study indicates that mercury interferes with thyroidal function in two ways: by interfering with the production of thyroidal hormones and by interfering with the conversion of T4 to T3.

Title

Effects of organic and inorganic mercurials on thyroidal functions.

Author

Kawada J; Nishida M; Yoshimura Y; Mitani K

Source

J Pharmacobiodyn, 3(3):149-59 1980 Mar

Abstract

Acute effects of methylmercuric chloride and mercuric chloride on thyroidal functions were examined. The organic *mercurial* concentration of $4 \times 10(-5)$ M inhibited by 50% of Na+K+ATPase in the membranous preparation from the hog thyroid, and $6 \times 10(-7)$ M of the inorganic *mercurial* showed the same extent of the inhibition. The Mg2+ ATPase activity in the preparation was neither affected by CH3HgCl up to a concentration of $2 \times 10(-3)$ M, nor by HgCl2 up to $1 \times 10(-4)$ M. After an intraperitoneal injection to mice of 5 micrograms of mercurial per gram body weight daily for 2 consecutive days, the 4-hour and the 24-hour uptakes of 131I by the thyroids were partially reduced by both organic and inorganic mercurials. A significant reduction in percentages of labeled iodothyronines was demonstrated to suggest that mercurial may cause a coupling defect in the synthesis of iodothyronines. Incubation of hog thyroglobulin with $8 \times 10(-3)$ M of methylmercuric chloride caused no observable aberration in slab disc electrophoreogram, but the protein was apparently denatured by the same concentration of mercuric chloride suggesting that thyroglobulin may carry a large binding capacity against either *mercurial*, but the inorganic *mercurial* can be more potent denaturant of the protein. The in vitro lysosomal hydrolysis of the *mercurial*-pretreated rat thyroglobulin which was labeled with 125I in vivo and fortified with the carrier hog thyroglobulin was not affected, but the direct addition of either *mercurial* in the medium resulted in a significant inhibition of the proteolytic action. Iodotyrosine deiodinase in the thyroid was inhibited by both *mercurials* in vitro and in vivo systems. A partial reduction in the serum bound 131I-iodide in both *mercurial* treated groups was observed at 4 hours and 24 hours after the radioiodide administration. The blood thyroxine levels estimated by radioimmunoassay were quite reduced in the inorganic mercurial treated group and also moderately reduced in the methylmercurial treated group, indicating that the hormone secretion was affected by mercurials.

In contrast to the above study this study found that mercury inhibited the production of T4 but didn't interfere with the conversion of T4 to T3. However, they didn't seem to control for selenium levels, which is probably important to do in these types of studies.

Title

Subacute toxicity of methylmercuric chloride and mercuric chloride on mouse thyroid.

Author

Nishida M; Yamamoto T; Yoshimura Y; Kawada J

Source

J Pharmacobiodyn, 9(4):331-8 1986 Apr

Abstract

Intoxication effect on mouse thyroid by prolonged administration of either CH3HgCl or HgCl2 was studied. It was found by giving CH3 203HgCl and 203HgCl2 through stomach intubation at either a single or a 30 d treatment that thyroid is a moderately susceptible organ to both *mercurials*. Animals were given 50, 100 and 150 micrograms/d of either *mercurial* in drinking water for a month. At the lowest amount of HgCl2, body weight was increased, whereas at the highest dose, there was a transient delay in growth. With lower amounts of CH3HgCl, no change in growth was observed. However, at the highest amount, a severe growth inhibition occurred. The thyroid weight was unaffected by lower amounts, but was significantly reduced by 150 micrograms/d of either *mercurial*. The 24 h radioiodide uptake in the thyroid, expressed by cpm/mg organ weight, was reduced by lower levels of *mercurials*. CH3HgCl and HgCl2 suppressed the rate of radioiodide incorporation into the iodothyronine fraction, but not into the iodotyrosine fractions, indicating that *mercurials* do not interfere with organification of iodide but do inhibit the coupling process. Serum thyroxine (T4) level was affected by mercurials, but serum triiodothyronine (T3) was not. This result suggested that even thyroidal secretion of T4 was inhibited by mercurials, but the peripheral conversion of T4 to T3 may not be affected in the maintenance of an active hormone level.

The following study shows that mercury interferes with the conversion of T4 to T3 in humans. Bear in mind that the majority (or all) of these workers are male and the effects of mercury on females may be ten times as high because of the acceleration effect of estrogen on mercury accumulation.

Title

Endocrine function in mercury exposed chloralkali workers.

Author

Barregard L; Lindstedt G; Schütz A; Sällsten G

Address

Department of Occupational Medicine, Sahlgren's University Hospital, S:t Sigfridsgatan, Göteborg, Sweden.

Source

Occup Environ Med, 51(8):536-40 1994 Aug

Abstract

OBJECTIVE--The aim was to study whether functional impairment of the pituitary, thyroid, testes, and adrenal glands of humans occupationally exposed to mercury (Hg) vapour can be shown as a result of accumulation of Hg in these glands. **METHODS**--Basal concentrations of thyrotrophin (TSH), prolactin, free thyroxine (free T4), free 3,5,3'-triiodothyronine (free T3), antibodies against thyroperoxidase, and testosterone in serum, as well as cortisol in morning urine were measured in 41 chloralkali workers exposed (10 years on average) to Hg vapour, and in 41 age matched occupationally unexposed referents. The chloralkali workers had a mean urinary Hg concentration (U-Hg) of 15 nmol/mmol (27 micrograms/g) creatinine, and a mean blood Hg concentration (B-Hg) of 46 nmol/l. For the reference group U-Hg and B-Hg were 1.9 nmol/mmol (3.3 micrograms/g) creatinine and 17 nmol/l respectively. **RESULTS**--**The serum free T4 concentration and the ratio free T4/free T3 were slightly, but significantly, higher in the subgroups with the highest exposure, and the serum free T3 was inversely associated with cumulative Hg exposure. This indicates a possible inhibitory effect of mercury on 5'-deiodinases, which are responsible for the conversion of T4 to the active hormone T3.** Serum total testosterone, but not free testosterone, was positively correlated with cumulative Hg exposure. Prolactin, TSH and urinary cortisol concentrations were not significantly associated to exposure. **CONCLUSION**--Apart from inhibition of the deiodination of T4 to T3, the endocrine functions studied seem not to be affected by exposure to Hg vapour at the exposure levels of the present study. Growth hormone secretion was not studied.

The following study, while it demonstrates species-specific differences, shows that mercury causes the production of autoantibodies in rats. Some of these autoantibodies are of the IgG class, which is known to be involved in autoimmune thyroid disease.

Title

Effects of HgCl₂ on the expression of autoimmune responses and disease in diabetes-prone (DP) BB rats.

Author

Kosuda LL; Greiner DL; Bigazzi PE

Address

Department of Pathology, University of Connecticut Health Center, Farmington 06030, USA.

Source

Autoimmunity, 26(3):173-87 1997

Abstract

Repeated exposure of Brown Norway (BN) rats to relatively low doses of HgCl₂ induces autoantibodies to renal antigens (e.g., laminin) and a membranous glomerulonephropathy characterized by proteinuria. In contrast, Lewis (LEW) rats are "resistant" to the autoimmune effects of mercury and, when exposed to this metal, are protected against experimental autoimmune encephalomyelitis (EAE) and Heymann's nephritis. To date, there is no information on "suppressive" effects of *mercury* in naturally occurring (so-called "spontaneous") rat models of autoimmune disease. Therefore, we have administered HgCl₂ to diabetes-prone (DP) BB rats, animals that spontaneously develop both insulin-dependent diabetes mellitus (IDDM) and thyroiditis. **We found that DP rats treated with mercury or water for a period of 40-125 days developed autoantibodies to thyroglobulin, with a higher incidence in HgCl₂-injected animals (92% vs. 56% in H₂O-injected controls).** A novel finding of our study was the detection of autoantibodies to laminin in the same rats, again with an increased incidence after HgCl₂ treatment (83% vs. 44%). **IgG2a was the most frequently detected isotype of antibodies to laminin, followed by IgG1, IgG2b and IgG2c.** The IgG isotype profile suggests that treatment with HgCl₂ may activate both Th1 and Th2 lymphocytes in BB rats. **In spite of these stimulatory effects on autoantibody responses, we found that there was no difference in the incidence of IDDM and thyroiditis between HgCl₂-treated and control animals.** We conclude that the suppressive effects of *mercury* previously observed in EAE and Heymann's nephritis of LEW rats do not occur in "spontaneous" autoimmune IDDM and thyroiditis of BB rats. Therefore, immune suppression caused by HgCl₂ cannot be considered a common phenomenon, but may be a genetically determined characteristic of LEW rats, possibly related to a specific or unique cytokine profile of this particular rat strain. **In contrast, while mercury does not seem to recruit, induce or rescue regulatory T cell function in DP rats, it does stimulate autoantibody responses in these animals.**

The following study demonstrates the long half-life of mercury in animals. Mercury was still detected in the thyroid gland of a dog exposed to mercury four years after the exposure ended.

Title

Distribution of dietary *mercury* in a dog. Quantitation and localization of total *mercury* in organs and central nervous system.

Author

Hansen JC; Reske-Nielsen E; Thorlacius-Ussing O; Rungby J; Danscher G

Address

Department of Toxicology, University of Aarhus, Denmark.

Source

Sci Total Environ, 78(1):23-43 1989 Jan

Abstract

An Alsatian dog which had been fed fish contaminated with methyl *mercury* for 7 years was examined after its death at the age of 12, 4 years after the exposure to methyl *mercury* had ceased. Two dogs of the same age and breed served as controls. In the exposed dog, *mercury* was found in all of the organs examined; the highest concentrations were found in the kidneys, and the lowest in the gastrointestinal tract and skeletal muscles. In the central nervous system (CNS) the *mercury* was fairly uniformly distributed, with 93% in the inorganic state, whereas the skeletal muscles contained approximately 30% inorganic *mercury*. This demonstrates time-dependent demethylation and suggests a variation in the rate from one type of tissue to another. At the time of death, the *mercury* level in the dog was still falling. In the control dogs, detectable amounts (0.01 mg kg⁻¹) of *mercury* were only found in the kidney and liver. The distribution of *mercury* was determined by a histochemical method (autometallography) for locating *mercury* in tissue sections. Sections from autometallography of the central nervous system showed large deposits of *mercury* in all areas of the cerebral hemispheres, the brainstem and the spinal cord, including nerve cells, astrocytes, microglial cells and vessel walls. The granular layer of the cerebellar hemispheres was especially loaded, while only a few granules were present in the Purkinje cells. In the leptomeninges the vessels and the macrophages were heavily encrusted. **High amounts of histochemically demonstrable mercury were observed in the liver, thyroid gland and kidney. In the control dogs, all the organs**

examined were practically devoid of deposits.

The following study demonstrates that not only does mercury bind to thyroidal tissues, but methylmercury has a preferential affinity for thiol groups. Thiols are an important part of antithyroidal drugs indicating that thiols are important in normal thyroidal functioning.

Title

Direct evidence for the presence of methylmercury bound in the thyroid and other organs obtained from mice given methylmercury; differentiation of free and bound methylmercuries in biological materials determined by volatility of methylmercury.

Author

Nishida M; Matsumoto H; Asano A; Umazume K; Yoshimura Y; Kawada J

Address

Faculty of Pharmaceutical Sciences, University of Tokushima, Japan.

Source

Chem Pharm Bull (Tokyo), 38(5):1412-3 1990 May

Abstract

Peroxidase in mouse thyroid was inhibited by mercuric chloride but not by methylmercury in in vivo and in vitro systems(Nishida, et al., J. Histochem. Cytochem., 37, 723 (1989)). To identify the reason for the difference, the present study was conducted to examine whether methylmercury is indeed bound within cells or tissues. Mice were given radioactive methylmercury by intubation for 18 d and the tissues were dissected out and vacuum-dried. With this procedure, free methylmercury was evaporated off and the bound *mercury* remained. The thyroid, liver, kidney and fats examined showed no loss of radioactivity under the vacuum, indicating that the **mercury was bound to the thyroid, as well as the other tissues**. Radioactive mercuric chloride was nonvolatile regardless of the presence or absence of the tissues. **The preferential affinity of methylmercury for SH-containing materials was re-confirmed by this method.**

The following two studies indicate that organic and inorganic forms of mercurials have different effects on the thyroid. Methyl mercury seems to interfere with the production of thyrotropin (TSH) so that the thyroid lowers production of hormone because of the lack of stimulation by thyrotropin. Inorganic mercury seems to inhibit the production of thyroid peroxidase (TPO) which causes the thyroid to increase production of thyroid hormone as a compensatory mechanism.

Title

Differential effects of methylmercuric chloride and mercuric chloride on the histochemistry of rat thyroid peroxidase and the thyroid peroxidase activity of isolated pig thyroid cells.

Author

Nishida M; Muraoka K; Nishikawa K; Takagi T; Kawada J

Address

Faculty of Pharmaceutical Sciences, University of Tokushima, Japan.

Source

J Histochem Cytochem, 37(5):723-7 1989 May

Abstract

This study was designed to characterize the interaction of CH₃HgCl or HgCl₂ with thyroid peroxidase (TPO). Two types of experiments were performed. First, the thyroids from rats that were given 5.6 mg/kg/day of either CH₃HgCl or HgCl₂ for 2 weeks by intubation were subjected to histochemical treatment and then to electron microscopy. TPO activities in all cell compartments were inhibited by HgCl₂ but not by CH₃HgCl. Morphological observation showed that taller epithelia were induced by HgCl₂, whereas flattened epithelia forming large follicles were induced by CH₃HgCl. **The serum thyrotropin level was substantially lowered by CH₃HgCl but was unchanged by HgCl₂.** Second, the guaiacol oxidation by TPO in isolated and ruptured pig thyroid cells was spectrophotometrically monitored in the presence of either CH₃HgCl or HgCl₂. **The TPO was not inhibited by CH₃HgCl but was inhibited by HgCl₂. These results indicated that CH₃HgCl induced a hypothyroid state without affecting TPO, whereas HgCl₂ inhibited TPO and induced a hypertrophic state** owing to compensation for loss of enzyme activity, and that the lack of inhibitory activity of CH₃HgCl was not due to the inability to penetrate the cells. **Therefore, there appeared to be a differential interaction of organic and inorganic forms of mercurials with the thyroid.**

Title

Differential effects of methylmercuric chloride and mercuric chloride on oxidation and iodination reactions catalyzed by thyroid peroxidase.

Author

Nishida M; Sato K; Kawada J

Address

Faculty of Pharmaceutical Sciences, University of Tokushima, Shomachi, Japan.

Source

Biochem Int, 22(2):369-78 1990 Oct

Abstract

Thyroid peroxidase (TPO), the major enzyme in the thyroid hormone synthesis, multifunctionally catalyzes (1) iodide oxidation, (2) iodination of the precursor protein, and (3) a coupling reaction of iodotyrosyl residues. The present study was carried out to examine the *mercurial* effects on the iodination, the second step of TPO. Purified porcine thyroglobulin or bovine serum albumin as acceptor protein was iodinated with [125I]NaI and H₂O₂ by purified porcine TPO. Iodinated protein was separated by acid precipitation on membrane filter or paper chromatography. Both CH₃HgCl and HgCl₂ dose-dependently inhibited the iodination, but HgCl₂ was more potent to inhibit the iodination than CH₃HgCl. These *mercurial* effects on the second step resemble the effects on the third step which were already reported; but are in marked contrast to the effects on the first step, where TPO was inhibited by HgCl₂ but never by CH₃HgCl.

The following study demonstrates how mercury can damage a fetus by interfering with the selenoenzymes and thyroid hormones.

In utero methylmercury exposure differentially affects the activities of selenoenzymes in the fetal mouse brain.

Watanabe C, Yoshida K, Kasanuma Y, Kun Y, Satoh H

Department of Environmental Health Sciences, Tohoku University Graduate School of Medicine, Seiryō-machi, Sendai, 980-8575, Japan.
chiho@humeco.m.u-tokyo.ac.jp

Pregnant ICR mice were subcutaneously injected with 0,5, or 3x3 mg Hg/kg of methylmercury (MeHg) on days 12,13, and 14(G12-14) of gestation and were sacrificed on G17. Activity of selenoenzymes, including glutathione peroxidase (GPx) and 5'- or 5-iodothyronine deiodinases (5'-DI, 5-DI), was determined in fetal brain and placenta. **MeHg did not affect the concentration of Se in these tissues, while it significantly inhibited the activity of GPx in the fetal brain and placenta, but not in the maternal brain. Although the levels of thyroid hormones in the maternal and fetal plasma were not affected by MeHg, 5-DI decreased and 5'-DI increased in the fetal brain, as if they had responded to hypothyroidism. Because the level of T4 in the fetal plasma was not affected by MeHg, these changes in enzymatic activities may result in a harmful excess of T3 in the fetal brain.** In addition, 5-DI activity was increased in the placenta of MeHg-treated mice. **These effects of prenatal MeHg exposure on fetal and placental DIs differed from those of dietary-induced Se deficiency, where the activities of DIs were decreased or not affected.** Further evaluation of the effect of MeHg on selenoenzymes, especially 5-DIs, is warranted. Copyright 1999 Academic Press.

In the following study the author states that ingestion of milk can increase the absorption of mercury up to 10 times. Other studies have shown that cadmium uptake can be increased significantly by simultaneous administration of estrogen. It's possible that it is the estrogen in milk which accounts for the accelerated accumulation of mercury from the diet. It is also stated that mercury in a mother is transferred to an infant through breast milk.

Z Ernährungswiss 1990 Mar;29(1):54-73

[The toxicological estimation of the heavy metal content (Cd, Hg, Pb) in food for infants and small children].

[Article in German]

Schumann K

Walther-Straub-Institut für Pharmakologie und Toxikologie der Ludwig-Maximilians-Universität, München, FRG.

There are differences between young and adult organisms regarding toxokinetic aspects and clinical manifestations of heavy metal intoxications. Chronically, toxic Cd intake causes a microcytotic hypochromic anemia in young rats at lower exposure levels and after shorter exposure periods than in adult animals. Cd absorption is increased by co-administration of milk and in conjunction with iron deficiency. After long exposure periods toxic Cd concentrations accumulate in the kidney cortex; this process starts very early in life. In 3-year-old children Cd concentrations in the kidney can reach up to one-third of those found in adults. **Hg++ and methyl-Hg can cause Hg encephalopathy, and frequently cause mental retardation in adults. Correspondingly, Hg++ accumulation in the brains of suckling rats is approx. 10 times higher than in grown animals. Milk increases the bioavailability of Hg++. In suckling rats Hg is bound to a greater extent to ligands in the erythrocytes. Methyl-Hg concentrations in breast milk reach 5% of those in maternal plasma and that is a severe hazard for breastfed children of exposed mothers.** Toxic Pb concentrations can lead to Pb encephalopathy. A high percentage of surviving children have seizures and show signs of mental retardation. Anemia and reduced intelligence scores were recently observed in children after exposure to very low levels of Pb. Pb absorption is increased in children and after co-administration of milk. There are no definite proofs for carcinogenesis or mutagenesis after oral exposure to Cd, Hg, and Pb in man. Heavy metal concentrations were found in the same order of magnitude in commercial infant formulas and in breast milk. When infant formulas are reconstituted with contaminated tap water, however, Pb and Cd concentrations can be much higher. The average heavy metal uptake from such diets exceeds the provisional tolerable weekly intake levels set by the WHO for adults, calculated on the basis of an average food intake and a downscaled body weight. These considerations do not even provide for differences in absorption and distribution or for the increased sensitivity of children to heavy metal exposure. However, dilution effects for essential heavy metals were observed in fast-growing young children; this effect might be extrapolated to toxic metals. These theoretical considerations are compared with epidemiological evidence. A health statistic from Baltimore shows a decline of Pb intoxications in infants. This observation correlates with a simultaneous decline in exposure to Pb which was due, for example, to decreased use of lead dyes in house paints and the abolition of tin cans for infant food.

Subject: Flu Shots and mercury

"According to Hugh Fudenberg, MD, the world's leading immunogeneticist and 13th most quoted biologist of our times (nearly 850 papers in peer review journals): If an individual has had 5 consecutive flu shots between 1970 and 1980 (the years studied) his/her chances of getting Alzheimer's Disease is 10 times higher than if he/she had one, 2 or no shots.

Dr. Fudenberg said it was so and that it was due to mercury and aluminum that is in every flu shot (and most childhood shots). The gradual mercury and aluminum buildup in the brain causes cognitive dysfunction. Is that why Alzheimer's is expected to quadruple.

Subj: [hyperthyroidism] hair analysis

Date: 3/23/00 7:30:25 PM Pacific Standard Time

From: cygnet@teleport.com (Swan)

Hi group. I got the hair analysis back. The only suggest was to add 2mg

of copper to the multi-vitamin, which I already do. It said my zinc shampoo could affect the reading for zinc, which was in the midline acceptable. Mercury is one asterick above the low level and it is suggested I look over the environment and water to help get it under control, but it isn't too bad. I am the one who eats fish for protein and have had these fillings in my teeth over 30 years. Chromium, which is know to contribute to diabetes (which leads to hypoT) hypoglycemia, and abnormal cholesterol, was below detection. It is suggested I begin supplement but warns it will take years to build up to acceptable. Selenium is detectable but supplementation is advised and takes years to build up. Lithium, which John says may contribute to hyperT, is undetectable but the lab doesn't say anything about it or cobalt. Vanadium is midline. I don't like that aluminum, lead, or cadium are detectable (but low). It suggests 500 calcium/300 mag that too much can lead to kidney stones. Still, I take 1000/500 and have just made midrange with both. I got this done at KingJames Lab 800-437-1404 for \$39.<http://www.kingjamesomegatech-lab.com/> Yes it was worth it too me. Also, the site has a neat thing about getting rid of mercury, at least for a period of time, called DMSA.

I am adding this so you get to find it if you don't do surfing well.

Thanks for showing interest. I don't think I am too concerned but certainly will include a single additional bottle of chromium to the already bunch of supplements of mine. Swan

DMSA

What is DMSA? DMSA is an abbreviation for 2,3-Dimercaptosuccinic Acid.

It is also marketed under the trade names "Chemet" and "Succimer." It is a FDA approved drug for treatment of lead toxicity in children. DMSA is also an excellent oral chelating agent for removing mercury from the body. It crosses the blood-brain barrier and removes toxic mercury from the brain and other body tissues. [See Aaseth, J. et al., Analyst, 120:853(1995)]

What is the Urine Mercury Test? A provocative dose of DMSA is provided by the lab along with a container for a 6-hour urine collection. When the analysis of the urine indicates significant levels of mercury are present, it is a signal that the body tissue levels are high.

What happens if the test result indicates high levels of mercury? If the mercury level is high, a prescription for DMSA can be given in conjunction with the removal of the source(s) of mercury contamination.

There are usually 25 capsules (500 mg each) in a prescription and one pill is taken three times a week for about 2 months.

What happens after the course of DMSA is concluded? It is recommended that a dentist knowledgeable in the proper procedure of amalgam filling removal be consulted within one month and mercury amalgam fillings be replaced with composite or gold. A dentist experienced in amalgam removal can be found by contacting either The International Academy of Oral Medicine and Toxicology (407-298-2450) or The Academy of Biological Dentistry (408-659-5385).

What happens if mercury amalgam fillings are not replaced? Although it is emphatically recommended that mercury amalgam fillings be properly replaced, if this is not done or is postponed, it is predictable that tissue levels of mercury in the body will build up again as mercury is constantly released from the teeth. In such cases, periodically repeating urine mercury testing and a course of DMSA chelation therapy is recommended.

Can DMSA be taken the day of and day after dental work involving mercury amalgam in order to remove any "stray" amalgam (mercury) from the body? Yes.

How is the DMSA obtained? The doctor will give the patient a prescription, then fax your prescription to a compounding pharmacy and give the patient a phone number to contact the pharmacy. The patient will need to contact the pharmacy directly with method of payment. The pharmacy will then air mail the DMSA to you.

Is it possible to present the prescription through prescription insurance plans or at another pharmacy? Retail pharmacies dispense the brand name "Chemet" form of DMSA in 1/5 the potency recommended. The compounding pharmacy provides the DMSA in a generic form that is substantially less costly than the Chemet. If Chemet is used, 5 times the amount needs to be taken. Insurance coverage may be applicable to compounding pharmacies; check with the pharmacy when you confirm the order.

Are there any side effects to using DMSA? There are usually little, if any, side effects to DMSA at the recommended dose. However, in some cases, as the body rids itself of the mercury, there could be some detoxification symptoms that might occur. If this is the case, the temporary ill effects of those symptoms are far less of a problem than the permanent ill effect of high levels of mercury in the tissue.

What kind of improvement should be noted using the DMSA? Most commonly, as the mercury is removed from the system, people will notice an improvement in short-term memory, sharper concentration, and a decrease in "foggy" thinking.

More information about mercury? See: Frackelton JP, Christensen, RL, "Mercury poisoning and its potential impact on hormone regulation and aging: Preliminary clinical observations using a new therapeutic approach," J. Advan. Med. 11:9-25(1998) and the HOT LINKS section of this web site.

Call the lab at (800)437-1404 to arrange for the submission of a specimen or for more details.

US EPA Proposes Regulations to Cut Mercury Emissions From Coal-Fired Power Plants - Carol Browner, head of the Environmental Protection Agency (EPA), said they would be proposing new regulations requiring coal-fired power plants to cut their toxic emissions of mercury. "Mercury from power plants settles over waterways, polluting rivers and lakes, and contaminating fish," she said in a statement. "The greatest source of mercury emissions is power plants, and they have never been required to control these emissions before now." Mercury is a highly toxic substance and can cause significant adverse health effects. Source: Mercola.com

The following is an article from Dr. Mercola's site, www.mercola.com, about the connection between mercury toxicity and autism. It basically states that the symptoms of autism are identical to the symptoms of mercury toxicity and that mercury toxicity is most likely the cause of autism. Infant get mercury toxicity from vaccinations because of the mercury-containing compound thimerosal. Thimerosal used to be used as a preservative in contact lens solution and may be in many other substances. Look at all products for thimerosal and any chemical with "mer" in it. This "mer" may indicate that it is a mercury compound. If you have children you don't want them to receive any vaccination with mercury in it.

Most likely mercury toxicity is involved in thyroid disease also, so as you read this article keep in mind that later in life this mercury load in the body can manifest as hypothyroidism or hyperthyroidism. Also remember that the best antidote to mercury toxicity is selenium.

Autism and Mercury

by Tim O'Shea, DC

This article is excerpted from Dr. O'Shea's forthcoming revised edition of *The Sanctity of Human Blood*.

Inquiry into vaccine safety is exploding like never before, even in the popular press. Research coming from dozens of mainstream medical studies can no longer be easily suppressed, as it has been in the past, especially with the prevalence of online information exchange.

Last September, some 2,000 people, mostly MDs, assembled at the Town and Country resort in San Diego to hear the latest research on autism. Following the April 2000 Congressional hearings on autism and vaccines, this epidemic can no longer be ignored.

The figure of one autistic infant for every 150 is now widely documented.

Dr. Stephanie Cave presented enlightening data on mercury toxicity, drawn largely from the brilliant work of Sallie Bernard. Dr. Cave explained how:

By age two, American children have received 237 micrograms of mercury through vaccines alone, which far exceeds current EPA "safe" levels of .1 mcg/kg. per day. That's one-tenth of a microgram, not one microgram.

Three days in particular may be singled out as spectacularly toxic for infants:

Day of birth: hepatitis B-12 mcg mercury

30 x safe level

At 4 months: DTaP and HiB on same day - 50 mcg mercury

60 x safe level

At 6 months: Hep B, Polio - 62.5 mcg mercury

78 x safe level

At 15 months the child receives another 50 mcg

41 x safe level

These figures are calculated for an infant's average weight in kilograms for each age.

These one-day blasts of mercury are called "bolus doses". Although they far exceed "safe" levels, there has never been any research conducted on the toxicity of such bolus doses of mercury given to infants all these years.

Inconceivable

Historically, the toxicity of mercury has been known for more than a century. The Mad Hatter was more than a fantasy character from Alice in Wonderland. Mad Hatter's disease became well known in England in the mid-1800s, when hat-makers were subject to inhaling the vapors from the mercury-based stiffening compound they used on felt to make top hats.

Sources of Mercury

It is interesting to learn that common household remedies that were used up into the 1960s like mercurochrome and "teething powder" were often the cause of acute mercury poisoning and disease.

In the U.S., EPA mercury toxicity studies have involved contamination from fish, air, and other environmental sources. This is inorganic mercury (methylmercury).

Methylmercury has long been associated with serious neurological disorders, demyelinating diseases, gut disease, and visual damage.

The mercury in vaccines, however, is in the form of thimerosal, which is 50 times more toxic than plain old mercury (methylmercury).

Reasons for this include:

- **Injected mercury is far more toxic than ingested mercury.**
- **There's no blood-brain barrier in infants.**
- **Mercury accumulates in brain cells and nerves.**
- **Infants don't produce bile, which is necessary to excrete mercury.**

Thimerosal is organic mercury

Once it is in nerve tissue, converted irreversibly to its inorganic form.

Thimerosal is a much more toxic form of mercury than one would get from eating open-sea fish; it has to do with the difficulty of clearing thimerosal from the blood.

Thimerosal is converted to ethylmercury, an organic form that has a preference for nerve cells.

Without a complete blood-brain barrier, an infant's brain and spinal cord are sitting ducks. Once in the nerve cells, mercury is changed back to the inorganic form and becomes tightly bound. Mercury can then remain for years, like a time-release capsule, causing permanent degeneration and death of brain cells.

Bernard also notes that the body normally clears mercury by fixing it to bile, but before six months of age, infants don't produce bile. Result: **mercury can't be excreted.**

Four separate government agencies have set safe levels for methylmercury, but no safe levels have ever been set for thimerosal, because thimerosal isn't included in toxicity studies.

Theoretically, that means that the above excesses of safe levels of mercury on the single days listed above are actually 50 times higher.

Does the fact that the mercury is accompanied by a vaccine somehow place it above scrutiny? The Sallie Bernard study of vaccines and mercury toxicity was probably the main reason Congress began to see the obvious correlation.

Mercury And Vaccines

Here's a curious "coincidence." In the late 1930s, Leo Kanner identified autism as a new type of mental disorder. So when was thimerosal introduced into vaccines?

The 1930s

A few years ago, Bernard and her associates began to notice a striking similarity between the symptoms of autism and the symptoms of mercury poisoning. The more research she did, the more it seemed that these two diseases were virtually identical.

Autism and mercury poisoning damage the: brain/nerve cells; eyes; immune system; gastrointestinal system; muscle control; and the speech center.

Although mercury toxicity has been studied for decades, and EPA safety levels have been set, during all that time a child's greatest exposure to mercury - thimerosal in vaccines - was never even included in the toxicity studies!

The talk has always been about methylmercury from seafood and the environment, totally ignoring the two most toxic sources of mercury for children: vaccines and dental amalgams.

The EPA has no jurisdiction over drugs.

That's the FDA's job. This is why vaccines and amalgams don't even figure into the equation when it comes to setting "safe" levels of mercury.

But the FDA does have jurisdiction over drugs and drug companies, right? And over drug company publications, like the Merck Manual, the standard cookbook for drugs and diseases found in every doctor's office in the world.

Surely the FDA, as the government agency charged with safeguarding the nation's health, would want the section on mercury toxicity to warn doctors about the two biggest sources for children: thimerosal and dental amalgams, wouldn't you think?

Yet looking at the Merck Manual (1999), in the section on mercury poisoning (p. 2636), thimerosal and dental amalgams again are not even mentioned!

How can this be, when mercury is widely acknowledged as the third most deadly toxin in the world and thimerosal and amalgams dwarf the trace amounts of mercury from fish and other environmental sources of mercury?

Only one thing can a blackout information over an entire area of study for years at a time in this way - **big money.**

Such an omission probably wouldn't have anything to do with the revolving door that exists between the FDA; the EPA; the NIH;

"and the sweet positions held by their members before and after those grueling years of public service; or with the 800 waivers of the conflict of interest rule that the FDA has granted in the past two years to "experts," who are paid consultants to the drug companies-consultants who are also members of the FDA advisory committees that make decisions about whether or not to approve vaccines and drugs..." (USA Today, Sept. 25, 2000)

No, of course not.

Soaking up the Mercury

In the San Diego conference on autism, Dr. Amy Holmes gave perhaps the only lucid presentation about treatment. She explained how chelating drugs alone, which go through the blood like Pac Man munching up mercury, don't do much good for autism.

That's because most mercury clears from the blood very soon. Mercury in thimerosal is stored in the gut, liver and brain, and as previously mentioned, becomes very tightly bound to the cells. Once inside those cells, or inside the blood-brain barrier, the mercury is reconverted back to its inorganic form.

Locked into these cells, the mercury can then do either immediate cell damage or become latent and cause the onset of autism, brain disorders, or digestive chaos years later.

Dr. Holmes reported success using alpha-lipoic acid as an agent to cross the blood-brain barrier to soak up mercury. Once the mercury is brought back into the bloodstream, standard chelators like DMSA can then take it out.

Dr. Holmes has used her protocol on about 300 autistics so far, and shows consistent increases in IQ scores.

FDA: Protector of Whom?

In the face of all this new awareness, it was astounding that in July 2000 the FDA came out with the "parallel-universe" pronouncement that "vaccines have safe levels of mercury."

Especially after their 1998 position:

"... over-the-counter drug products containing thimerosal and other mercury forms are not generally recognized as safe and effective."

As if there were any doubt as to who's really running the show, inconceivable also is the impotence of FDA's request to the vaccine manufacturers to discontinue the use of thimerosal in vaccines ([LINK TO ARTICLE ON SITE](#)) The same month that MMWR published this, the CDC made the same milquetoast request.

It's a bit like saying: "Hey guys, since all these kids are turning into vegetables and most of our researchers know it's the mercury, would you mind not putting any more thimerosal in your vaccines, please?"

No hurry, though. Whenever you're ready. No need to dump all those batches of vaccine just because people are finding out it's the mercury that's destroying children's brain cells."

The members of the FDA who decide which vaccines get approved make up the advisory board. In his recent House investigation on vaccines, Rep. Dan Burton found out that financial statements of advisory board members are "incomplete."

Noting that this is the only branch of government that allows incomplete financials, in September 2000, Burton called the advisory board's sweetheart arrangements with the vaccine manufacturers a "violation of the public trust."

This includes 70 percent of advisory board members owning stock in vaccines, owning patents on vaccines, and accepting salaries and benefits as employees of the drug companies.

A Matter of Trust

Still think you can trust the government or your physician with your children's blood? Despite the facts and events cited above, consider this joint statement of the U.S. Public Health Services and the American Academy of Pediatrics:

"There is a significant safety margin incorporated into all the acceptable mercury exposure limits. There are no data or evidence of any harm caused by the level of exposure that some children may have encountered in following the existing immunization schedule ... Infants and children who have received thimerosal-containing vaccines do not need to be tested for mercury exposure" ([TRY TO REPLACE THIS WITH LINK FROM SITE MMWR, vol. 45, 1999](#)).

These are blatant Orwellian distortions. No harm?

- **What about the autism epidemic and all the evidence linking it with mercury cited above?**
- **What about the single day doses of mercury cited above that are dozens of times in excess of the EPA's own safety levels?**
- **If everything is so safe, then why did they ask the vaccine pushers to kindly discontinue thimerosal from vaccines as soon as possible at the end of this same statement?**

It is beyond the scope of this paper to really go into the politics of mercury. In researching mercury toxicity, a whole area of "dry rot" has been unearthed that deserves its own story. This is the shocking story of how the American Dental Association and the California Dental Association have been systematically hiding the truth about mercury toxicity in fillings for decades.

Silver fillings aren't just silver. They're 50 percent mercury and extremely toxic; every dentist knows it (www.altcorp.com, <http://www.amalgam.org/>).

In a ludicrous blast of irony, both the ADA and the CDA have inserted into their "code of ethics" strict commandments forbidding dentists from ever revealing to patients the realities of mercury toxicity.

No dentist is allowed to recommend removal of mercury amalgams for health reasons, nor may tell the patient about mercury toxicity even if the patient asks. This gag order has been in place for since the beginning of American dentistry. Exaggeration? Check their websites out:

www.amalgam.org/#anchor69176 www.amalgam.org/#anchor69541

Do you think dentists put mercury into their own families' teeth? Ask them. Anyone who is not a dentist is not constrained by the gag order, imposed on American dentists by the ADA, against telling patients what many perceptive researchers in the field of mercury toxicity already know: that no children should ever get mercury amalgam fillings.

Laughingstock of the West

Researchers across Europe are generally appalled at the massive amounts of vaccines given to American children under two years old. Although Europeans are not as obsessed with vaccines as we are, they do vaccinate.

But most of Europe gives very few vaccinations to children under two years old, primarily because of the unformed gut, immune system, and blood-brain barrier.

This intellectual isolation of ours regarding vaccines is a testimony to the suffocating "brain control" exerted on us by the popular press and all media. Like sheep to the slaughter, we don't know enough to be appalled by our own ignorance.

Autistic Gut

Headlining the September 2000 San Diego Conference was Andrew Wakefield, the British surgeon whose shocking new discoveries show that mercury toxicity alone is not the only factor linking vaccines with the autism epidemic. Dr. Wakefield's research centers around the MMR vaccine - measles/mumps/rubella - which does not contain thimerosal.

Expanding on his presentation at the April 2000 Burton hearings, Dr. Wakefield explained how at least three-quarters of autistics have pathologically blocked bowels, due to the huge swelling of the tissue lining the intestine.

In virtually every autistic patient they examined, this nodular hyperplasia is both an immune response and an autoimmune response that Wakefield and O'Leary have clearly linked to the presence of measles virus from the MMR shot. No other virus was found in those cells.

It is a new bowel pathology.

Wakefield showed graphs of the U.S. and U.K. 10 years apart that were identical in tracing the skyrocketing incidence of autism just after the MMR vaccine was introduced.

He also showed how the incidence of measles had dropped over 85 percent on its own before the MMR was introduced.

One incredible study cited by Wakefield showed how 76 percent of children whose mothers were exposed to atypical measles became autistic after the MMR shot! He called this a "background susceptibility" or predisposition to autism.

Wakefield reminds us that in neither country have there ever been comparative studies on giving multiple vaccines (polyvalent) on the same day.

This custom of ours, with both the DPT and the MMR, is not scientific by any stretch, and is primarily for the convenience of those administering the shots, and those being paid per vaccine. As a result, there is a good chance of geometric ill effects.

Then Wakefield cited the original MMR study (Buynak, Journal of the American Medical Association 1969, vol. 207).

Not only was the safety of multiple vaccines never mentioned, there was no follow-up to the study to see if their conclusions were correct.

In the usual manner of testing vaccines on the live population, MMR was simply tacked onto the mandatory schedule, and we've never looked back.

Despite studies in 1981 on Air Force personnel showing major synergistic adverse effects in the gut from the combination of measles and rubella vaccines, the mandatory schedule went unchanged.

A Glimmer of Hope

Despite these formidable obstacles, doubts are creeping into the overall public "consciousness" about the safety of vaccines. At one in 150, the fact of autism as an epidemic can no longer be covered up.

The work of Wakefield, O'Leary, Megson and Bernard is getting more and more difficult to explain away. Rep. Dan Burton seems relentless in his efforts to acquaint Congress with the meretricious relationship between the FDA Advisory Committee and the vaccine manufacturers.

The massive advertising campaign about the safety of vaccines in the popular media, which is certain to be stepped up in the next few months, is going to look very hollow in the light of clean, unbiased research that is not funded by parties who stand to make billions from certain predetermined results.

And the internet makes this well-referenced, scientific work accessible to the public without the usual monodimensional smokescreen from the popular press.

Ultimately, the value of the San Diego "Conference on Autism" was its signal that autism will not be allowed to slip from the public awareness, like so many other feature stories that come and go. The simple truth has been unveiled, and anyone who looks can see it clearly: our prime question should not be asking how we can cure autism once it occurs. The evidence is now overwhelming that in most cases, this new epidemic that we call autism is a preventable disease.

DR. MERCOLA'S COMMENT:

Congratulations to Dr. O'Shea for an excellent review of this important topic.

Related Articles:

[Autism and Mercury Detoxification](#)

[Autism: a Novel Form of Mercury Poisoning](#)

[Studies on the Effects of Secretin in Children With Autism](#)

[Single Injection Of Secretin Does Not Treat Autism](#)

[Objections to the Study That Showed Secretin Does Not Work for Autism](#)

[Short-Term Benefit In Treating Autism With Antibiotics](#)

[The Neurobiology of Lipids In Autistic Spectrum Disorder](#)

[Link Between Autism and Vaccination](#)

[Autism May Be Caused By an Immune System Response To a Virus](#)

[Vaccine - Autism Link Feared](#)

[Vaccine Induced Autism](#)

[Milk Link To Autism](#)

The following article on mercury is from Dr. Mercola's website, mercola.com:

Mercury Toxicity and Systemic Elimination Agents

The following paper has been a long time in the making. I first wrote it nearly three years ago and it was initially rejected by the Lancet and the British Medical Journal but was published last month in the Journal of Nutritional and Environmental Medicine (March 2001).

The end of the article has the bibliography which took quite awhile to compile and has 124 of the best literature documentation I could find on mercury detoxification.

For a practical summary of the paper and exactly what one should do, please review my [mercury detoxification protocol](#).

Dr. Klinghardt is widely recognized as one of the most knowledgeable physicians in mercury detoxification and it was a privilege to be able to help him with this paper.

The timing is especially appropriate in light of the [mercury lawsuit that was filed last week](#)

Later this month on April 24 I will be involved in a press conference that will announce massive additional lawsuits relating to the toxicity of mercury. These lawsuits have the potential to make the tobacco issue look like small potatoes as the liabilities could run in the trillions of dollars.

Abstract

This paper reviews the published evidence supporting amalgam toxicity and describes practical and effective clinical techniques that facilitate mercury elimination. A literature review is provided which documents effective mercury elimination strategies to reduce mercury toxicity syndromes.

Considering the weight of evidence supporting mercury toxicity, it would seem prudent to select alternate dental restoration materials and consider effective mercury elimination strategies if mercury toxicity is present.

Mercury Exposure And Toxicity Is A Prevalent And Significant Public Health Threat.

Chronic mercury exposure from occupational, environmental, dental amalgam, and contaminated food exposure is a **significant threat to public health**.¹

Those with amalgam fillings **exceed all occupational exposure allowances** of mercury exposure of all European and North American countries. Adults with four or more amalgams run a significant risk from the amalgam, while in children as few as two amalgams will contribute to health problems.² In most children, the largest source of mercury is that received from immunizations^{3 4 5 6} or that transferred to them in utero from their mother.^{7 8}

Dental Amalgams Are A Major Source Of Mercury Toxicity

A single dental amalgam filling with a surface area of only 0.4 sq.cm is estimated to release as much as 15 micrograms of mercury per day primarily through mechanical wear and evaporation.^{1 9 10 11}

The average individual has eight amalgam fillings and could absorb up to **120 micrograms of mercury per day** from their amalgams. These levels are consistent with reports of 60 micrograms of mercury per day collected in human feces.¹² By way of contrast, estimates of the daily absorption of all forms of mercury from fish and seafood is 2.3 micrograms and from all other foods, air and water is 0.3 micrograms per day.¹³ Currently, Germany, Sweden and Denmark severely restrict the use of amalgams.¹

A "silver" filling, or dental amalgam, is not a true alloy. Amalgams are made up of **50% mercury**. The amalgam also consists of 35% silver, 9% tin, 6% copper and a trace of zinc.⁶ More than 100 million mercury fillings are placed each year in the U.S. as over **90% of dentists use them** for restoring posterior teeth.¹⁴

The mercury vapor from the amalgams is lipid soluble and passes readily through cell membranes and across the blood brain barrier.¹⁵ The vapor serves as the primary route of mercury from amalgams into the body. It is clear that amalgam mercury transfers to human tissues, accumulates with time, and presents a **potential health threat**. The mercury escapes continuously during the entire life of the filling primarily in the form of vapor, ions but also abraded particles.^{16 17} Chewing, brushing, and the intake of hot fluids stimulates this release.^{18 19 20}

Statements made by dental authorities which claim that the amount of mercury exposure encountered by patients from dental amalgams is too small to be harmful, are contradicted by the literature.²¹

Animal studies show that radioactively labeled mercury released from ideally placed amalgam fillings appear quickly in the kidneys²², brain and wall of the intestines.²³ The fact that mercury amalgam fillings are **banned in some European countries** is strong evidence of the clinical toxicity of this material.

Any metal tooth restoration placed in the mouth will also produce electrogalvanic effects. When dissimilar metals are placed in the oral cavity they exert a battery-like effect because of the electroconductivity of the saliva. The electrical current causes metal ions go into solution at a much higher rate, thereby increasing the exposure to mercury vapor and mercury ions manyfold. Gold placed in the vicinity of an amalgam restoration produces a 10-fold increase in the release of mercury.²⁴

Mercury's Long Half-Life In The Central Nervous System

Mercury in the central nervous system (CNS) causes psychological, neurological, and immunological problems in humans.^{25 26 27} Mercury bonds very firmly to structures in the CNS through its affinity for sulfhydryl-groups on amino acids. Other studies have shown that mercury is taken up in the periphery by all nerve endings and rapidly transported inside the axon of the nerves (axonal transport) to the spinal cord and brainstem.^{28 29 30} Unless actively removed, mercury has an extremely long half-life of somewhere between **15 and 30 years** in the CNS.^{1 31}

Mercury Toxicity Symptoms

The overt clinical effects resulting from toxic exposure to mercury have been clearly described.^{32 33} The scientific literature shows that amalgam fillings have been associated with a variety of problems such as Alzheimer's Disease,^{34 35} autoimmunity,^{36 37 38} kidney dysfunction,³⁹ infertility,^{40 41 42} polycystic ovary syndrome,⁴³ neurotransmitter imbalances,⁴⁴ food allergies,⁴⁵ multiple sclerosis,⁴⁶ thyroid problems,⁴⁷ and an impaired immune system.⁴⁸

Patients with many amalgam fillings will also have an increase in the prevalence of antibiotic resistant bacteria.⁴⁹ Subclinical neuropsychological and motor control effects were also

observed in dentists who had documented high mercury exposure levels.^{50 51} Amalgam use may also be related to fatigue, poor memory and certain psychological disorders.⁵²

There has been a recent epidemic of autism in the US^{3 54} and many investigators believe that this may be partially related to the increased exposure infants have had to mercury through the preservative thimerosal that was included in nearly all vaccines until recently.⁵⁵

The **nervous system** is more sensitive to mercury toxicity than any other organ in the body. Mercury has recently been documented to be associated with **arrhythmias** and **cardiomyopathies** as hair analysis showed mercury levels to be 20,000 higher in those with these cardiac abnormalities.⁵⁶ Mercury exposure has also been associated with other neurological problems such as tremors,⁵⁷ insomnia, polyneuropathy, paresthesias, emotional lability, irritability, personality changes, headaches, weakness, blurred vision, dysarthria, slowed mental response and unsteady gait.^{1 58 59}

Systemic Mercury Elimination

There are a number of agents that have been demonstrated to have clinical utility in facilitating the removal of mercury with someone who has demonstrated clinical signs and symptoms of mercury toxicity. The urine and feces are the main excretory pathways of metallic and inorganic mercury in humans.^{1 60}

The most important part of systemic elimination is to **remove the source of mercury**.

For most this involves amalgam removal. Individuals should seek a dentist who is specially trained in this area as improperly removed amalgam may result in unnecessarily high exposure to mercury.⁶¹ The following is a summary of the most effective agents that have been documented in the peer-reviewed literature.

DMPS

DMPS (Sodium 2,3-dimercaptopropane-1-sulfonate) is an acid-molecule with two free sulfhydryl groups that forms complexes with heavy metals such as zinc, copper, arsenic, mercury, cadmium, lead, silver, and tin. DMPS was developed in the 1950s in the former Soviet Union and has been used to effectively treat metal intoxication since the 1960s there.⁶² It is a water-soluble complexing agent.

Because it had potential use as an antidote for the chemical warfare agent, Lewisite, it was not available outside of the Soviet Union until 1978, at which time Heyl, a small pharmaceutical company in Berlin, Germany started to produce it. It has an abundance of international research data and an **excellent safety record in removing mercury** from the body⁶³ and has been used safely in Europe as Dimaval for many years.^{64 65 66 67}

DMPS is registered in Germany with the BGA (their FDA) for the treatment of mercury poisoning but is still an investigational drug in the United States.⁶⁸

The best and only brand of DMPS that should be used is Heyl from Germany. Great care should also be exercised in making certain the DMPS is compounded properly from the pharmacist. If the DMPS contacts metal during it will be oxidized, so the compounding pharmacist must use nonmetal needles must be used in preparing the product.

DMPS Can Be Used To Eliminate Mercury Systemically

The use of DMPS to treat mercury toxicity is well established and accepted.^{69 70 71} DMPS has clearly demonstrated elimination effects on the connective tissue.^{72 73} The DMPS dose is 3-5 mg /kg of body weight once a month which is injected slowly intravenously over five minutes. DMPS-stimulated excretion of all heavy metals reaches a maximum 2-3 hours after infusion and decreases thereafter to return to baseline levels after 8 hours.⁷⁴

DMPS Safety

DMPS is not mutagenic, teratogenic or carcinogenic⁷⁵ Ideally intravenous DMPS should never be used in patients that still have amalgam fillings in place, although investigators have done this as diagnostically, as a one-time dose, without complications.⁷⁶ DMPS appears in the saliva and may mobilize significant amounts of mercury from the surface of the fillings and precipitate seizures, cardiac arrhythmias, or severe fatigue.

One should use DMPS with great caution and **NEVER** use it in patients with amalgam fillings. Ideally DMPS should be administered after 25 grams of ascorbic acid administered intravenously. This will minimize any potential toxicity from the DMPS.

Even though DMPS has a high affinity for mercury, the highest affinity appears to be for

copper and zinc⁷⁷ and supplementation needs to be used to not avoid depleting these beneficial minerals. Zinc is particularly important when undergoing mercury chelation.⁷⁸ DMPS is administered over a five-minute period since hypotensive effects are possible when given intravenously as a bolus.^{79 80} Other possible side effects include allergic reactions and skin rashes.

DMSA

DMSA (meso-2, 3-dimercaptosuccinic acid) is another mercury chelating agent. It is the only chelating agent other than cilantro and d-penicillamine⁸¹ that penetrates brain cells. DMSA removes mercury both via the kidneys and via the bile.⁸² The sulfhydryl groups in both DMPS and DMSA bind very tightly to mercury.

DMSA has three distinct disadvantages relative to DMPS.

First, DMPS appears to remain in the body for a longer time than DMSA.⁸³

Secondly, DMPS acts more quickly than DMSA, probably because its distribution is both intracellular and extracellular.⁸⁴

Thirdly, preparations of DMPS are available for intravenous or intramuscular use, while DMSA is available only in oral form.⁸⁵ Since succinic acid is used in the citric acid cycle inside the cell, DMSA has been suspected for displacing mercury towards the inside of the cell⁸⁶ after binding mercury somewhere on its way from the intestine to the succinic acid deficient cell.

We propose therefore that DMSA be **used late in the mercury elimination process**, after the connective tissue mercury load has been reduced with DMPS. The standard dose of DMSA is 5-10 mg/kg twice a day for two weeks. The DMSA is then stopped for two weeks and then the cycle is repeated.

Chlorella

Algae and other aquatic plants possess the capacity to take up toxic trace metals from their environment, resulting in an internal concentration greater than those of the surrounding waters.⁸⁷ This property has been exploited as a means for treating industrial effluent containing metals before they are discharged, and to recover the bioavailable fraction of the metal.⁸⁸

Chlorella has been shown to develop resistance to cadmium contaminated waters by synthesizing metal-binding proteins.⁸⁹ A book written for the mining industry, *Biosorption of Heavy Metals*,⁹⁰ details how miners use these organisms to increase the yield of precious metals in old mines. The mucopolysaccharides in chlorella's cell wall absorb rather large amounts of toxic metals similar to an ion exchange resin.

Chlorella also enhances mobilization of mercury compartmentalized in non-neurologic structures such as the gut wall,⁹¹ muscles, ligaments, connective tissue, and bone.

High doses of chlorella have been found to be very effective in Germany for mercury elimination.⁹²

Chlorella is an important part of the systemic mercury elimination program, as approximately 90% of the mercury is eliminated through the stool. Using large doses of chlorella facilitates fecal mercury excretion. After the intestinal mercury burden is lowered, mercury will more readily migrate into the intestine from other body tissues from where **chlorella will effectively remove it**.

Chlorella is not tolerated by about one-third of people due to gastrointestinal distress. Chitosan can be effectively used as an alternative in these individuals. Chitosan makes up most of the hull of insects shellfish and also bind metals like mercury from the lumen of the intestines.^{93 94 95}

Cilantro

Omura determined that cilantro could mobilize mercury and other toxic metals rapidly from the CNS.^{96 97}

Cilantro mobilizes mercury, aluminum, lead and tin stored in the brain and in the spinal cord and moves it into the connective tissues. The mobilized mercury appears to be either excreted via the stool, the urine, or translocated into more peripheral tissues.

The mechanism of action is unknown. Cilantro alone often does not remove mercury from the

body; it often only displaces the metals from intracellularly or from deeper body stores to more superficial structures, from where it can be easier removed with the previously described agents. The use of cilantro with DMSA or DMPS has produced an increase in motor nerve function.⁹⁸

Potentiating Agents

Adequate sulfur stores are necessary to facilitate mercury's binding to sulfhydryl groups.

Many individual's sulfur stores are greatly depleted which impairs sulfur containing chelating or complexing agents, such as DMPS or DMSA, effectiveness as they are metabolized and utilized as a source of sulfur. Sulfur containing natural substances, like garlic^{99 100} and MSM (methylsulfonylmethane) may also serve as an effective agent to supply organic sulfur for detoxification.¹⁰¹ Fresh garlic is preferred as it has many other recently documented benefits.^{102 103 104} The garlic is consumed just below the threshold of social unacceptability, which is typically 1-2 cloves per day.

Antioxidants

Vitamin E doses of 400 I.U per day have been shown to have a **protective effect** when the brain is exposed to methyl-mercury.^{68 105} Selenium, 200-400 mcg daily,^{106 107 108 109} is a particularly important trace mineral in mercury elimination and should be used for most patients.

Selenium facilitates the function of **glutathione**, which is also important in mercury detoxification.^{110 111 112} Some clinicians find repetitive high dose intravenous glutathione useful, especially in neurologically compromised patients.

There is a suggestion in a rat model that lipoic acid may also be useful,¹¹³ but some clinicians are concerned about the potential of lipoic acid to bring mercury into the brain early in the stages of chelation, similar to DMSA and N-acetylcysteine (NAC), which has also been used in mercury chelation.¹¹⁴ Doses larger than 50-100 mg per day should be used with caution.

Vitamin C is also a helpful supplement for mercury elimination as it will tend to mobilize mercury from intracellular stores.^{115 116 117 118 119 120}

Some clinicians will use it intravenously in doses of 25-100 grams IV in preference to DMPS and DMSA.

Hyaluronic acid (HA) is a major carbohydrate component of the extracellular matrix and can be found in the skin, joints, eyes and most other organs and tissues.¹²¹ HA is utilized in many chemotherapy protocols as a potentiating agent.¹²² HA is also being utilized for many novel applications in medicine.^{123 124} Personal experience has shown that the addition of 2 ml with the DMPS tends to improve the excretion of mercury by two to four fold with **virtually no toxicity**.

Conclusion

We have described the significant toxicities associated with mercury amalgams and treatment agents that both authors have used successfully over the past two decades to eliminate mercury and resolve many chronic health complaints. Considering the weight of evidence supporting amalgam toxicity it would seem prudent to select alternative dental restoration materials.

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MILK

Many hypers find that milk increases hyper symptoms. The high amounts of calcium versus magnesium in milk may be the reason for this observation but there may be another reason: estrogen.

Estrogen is found in milk and studies have shown that estrogen increases cadmium absorption. I believe that cadmium is a major promoter of Graves' disease and TED and the effects of estrogen on cadmium (and possibly other metal) absorption may be the major factor explaining why women get thyroid disease at a much higher rate than men.

Following is a study which states that cadmium toxicity causes anemia, a condition highly associated with thyroid disease. As the article states, cadmium "absorption is increased by co-administration of milk and in conjunction with iron deficiency."

Quoting the study, "Hg⁺⁺ accumulation in the brains of suckling rats is approx. 10 times higher than in grown animals. Milk increases the bioavailability of Hg⁺⁺." Does this "10 times" strike a bell for you as it does for me? This is the factor by which women (high in estrogen) are more likely to get hyperthyroidism than men.

The evidence is clearly pointing to heavy metal toxicity from cadmium and mercury which is accelerated by estrogen as the causative factor for hyperthyroidism and hypothyroidism. Milk consumption may be one of the ways that estrogen levels are increased in the body and cadmium absorption is magnified.

Z Ernährungswiss 1990 Mar;29(1):54-73

[The toxicological estimation of the heavy metal content (Cd, Hg, Pb) in food for infants and small children].

[Article in German]

Schumann K

Walther-Straub-Institut für Pharmakologie und Toxikologie der Ludwig-Maximilians-Universität, München, FRG.

There are differences between young and adult organisms regarding toxokinetic aspects and clinical manifestations of heavy metal intoxications. **Chronically, toxic Cd intake causes a microcytotic hypochromic anemia in young rats at lower exposure levels and after shorter exposure periods than in adult animals. Cd absorption is increased by co-administration of milk and in conjunction with iron deficiency.** After long exposure periods toxic Cd concentrations accumulate in the kidney cortex; this process starts very early in life. In 3-year-old children Cd concentrations in the kidney can reach up to one-third of those found in adults. **Hg⁺⁺ and methyl-Hg can cause Hg encephalopathy, and frequently cause mental retardation in adults. Correspondingly, Hg⁺⁺ accumulation in the brains of suckling rats is approx. 10 times higher than in grown animals. Milk increases the bioavailability of Hg⁺⁺.** In suckling rats Hg is bound to a greater extent to ligands in the erythrocytes. Methyl-Hg concentrations in breast milk reach 5% of those in maternal plasma and that is a severe hazard for breastfed children of exposed mothers. Toxic Pb concentrations can lead to Pb encephalopathy. A high percentage of surviving children have seizures and show signs of mental retardation. **Anemia and reduced intelligence scores were recently observed in children after exposure to very low levels of Pb.** Pb absorption is increased in children and after co-administration of milk. There are no definite proofs for carcinogenesis or mutagenesis after oral exposure to Cd, Hg, and Pb in man. Heavy metal concentrations were found in the same order of magnitude in commercial infant formulas and in breast milk. When infant formulas are reconstituted with contaminated tap water, however, Pb and Cd concentrations can be much higher. The average heavy metal uptake from such diets exceeds the provisional tolerable weekly intake levels set by the WHO for adults, calculated on the basis of an average food intake and a downscaled body weight. These considerations do not even provide for differences in absorption and distribution or for the increased sensitivity of children to heavy metal exposure. However, dilution effects for essential heavy metals were observed in fast-growing young children; this effect might be extrapolated to toxic metals. These theoretical considerations are compared with epidemiological evidence. A health statistic from Baltimore shows a decline of Pb intoxications in infants. This observation correlates with a simultaneous decline in exposure to Pb which was due, for example, to decreased use of lead dyes in house paints and the abolition of tin cans for infant food.

Ann N Y Acad Sci 1986;464:75-86

Hormones in milk.

Schams D, Karg H

Protein hormones (especially prolactin) and steroid hormones (gestagens, estrogens, corticoids, and androgens) can be detected by bioassay and radioimmunoassay in milk in a variety of species. In addition, milk contains vitamin D and beta-casomorphins (opiate-like peptides). It has been assumed that most of the hormones are transferred into milk by diffusion. However, evidence is available for active mechanisms like those for progesterone in goats and prolactin in cows. Most of the hormone profiles in milk are similar to the ones in blood plasma. Hormone concentrations in milk seem to be a good estimate of the average hormone content in plasma, especially for the measurement of longer-lasting secretory activities like progesterone and estrogen release during the estrous cycle or seasonal changes of prolactin in ruminants. Determination of progesterone and estrone sulfate in milk serves as a diagnostic tool in fertility control, especially in cows. Enzyme immunoassay kits are available for this monitoring purpose. Exogenously administered hormones are also transferred into milk. Residue studies have shown that the dilution is so great that it may be assumed that there is no potential risk for the consumer.

Prog Food Nutr Sci 1990;14(1):1-43

A review of the hormone prolactin during lactation.

Ostrom KM

The principal lactogenic hormone, prolactin, secreted by the anterior pituitary is critical to the establishment of lactation, milk macronutrient content and milk production. The concentration of circulating prolactin increases during pregnancy so that by the end of gestation, levels are 10 to 20 times over normal amounts. However, prolactin is prevented from exerting its effect on milk secretion by elevated levels of progesterone. Following clearance of progesterone and estrogen at parturition, copious milk secretion begins. The minimal hormonal requirements for normal lactation to occur are prolactin, insulin and hydrocortisone. Prolactin stabilizes and promotes transcription of casein mRNA; may stimulate synthesis of alpha-lactalbumin, the regulatory protein of the lactose synthetase enzyme system; and increases lipoprotein lipase activity in the mammary gland. Prolactin levels decrease as lactation is established but nursing stimulates prolactin release from the pituitary which promotes continued milk production. Prolactin is secreted into milk at levels representative of the average circulating concentration. The physiological significance of milk prolactin to the infant is uncertain. Prolactin exists in three heterogenic forms which possess varying biological activity. The monomer with a molecular weight of 23 kDa is found in greatest quantity and is the principal biologically active form. The pattern of heterogeneity changes during pregnancy to favor even more monomer in proportion to the dimer. However, during lactation, the proportion of the monomer in circulation decreases in response to selective uptake of the monomer by the mammary gland. Over 90 percent of the prolactin in milk is present as the monomer. Prolactin may exert some of its biological effect by a shift in the ratio of active to less active forms of the molecule.

Med Hypotheses 1997 Jun;48(6):453-61

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Dairy products and breast cancer: the IGF-I, estrogen, and bGH hypothesis.

Outwater JL, Nicholson A, Barnard N

A. B. Princeton University 1996, Physicians Committee For Responsible Medicine, Washington, DC 20016, USA.

Research on the role of dietary factors in breast cancer causation has focused predominantly on fat intake. While some studies have examined associations between breast cancer rates and consumption of whole milk, there has been less attention given to dairy products in general. Dairy products contain both hormones and growth factors, in addition to fat and various chemical contaminants, that have been implicated in the proliferation of human breast cancer cells. This literature review evaluates the epidemiological and mechanistic evidence linking dairy consumption with breast cancer risk.

In a message dated 11/3/00 8:59:09 AM Pacific Standard Time, getdawnrose@hotmail.com writes:

<< Several studies have reported a seasonal variation in the presentation of patients with Graves' disease. This was observed in European studies dating back to the 1920s as well as more recent studies from the United States, the United Kingdom, and New Zealand . These studies suggest that cases tend to present in the spring and early summer months both in the Northern and the Southern hemisphere. The most obvious explanation of this trend is that higher summer causes the symptoms of hyperthyroidism to be less well tolerated so that patients are more likely to seek medical attention. However, there are other possible explanations. In a study in the UK it appeared that the onset as well as the the presentation of the disease was seasonal with a peak period of onset from January to June. It was suggested that a winter increase in the iodine content of the diet could have triggered the disease in some patients. The winter increase in dietary iodine intake is well recognized in Northern European countries and is due to the practice of supplementing cattle feed with iodine during the winter months.">>

Hi Dawn,

There are probably some very logical explanations of why hyperT increases in the late winter to the summer. I was unaware that iodine supplementation for cattle was increased during the winter, but this would probably mean higher iodine content in milk. We know that milk is a real negative for hypers and I know of three reasons: (1) Milk cans at the dairy are cleaned with iodine and there is always some retained in the can, (2) The milk cans are galvanized which means that zinc and cadmium get into the milk from the can and both these metals are copper antagonists, and (3) Milk is extremely low in copper.

Humans drink milk for vitamin D and vitamin D status declines to a minimum in February. Since it is an oil vitamin, it is stored in the body from the prior fall, but people run very low by Jan-March. Increased milk and dairy consumption to get vitamin D increases the hyper promoting effects of milk consumption

Also, in spring and summer, people start eating more fruit. Fruit is another negative for hypers because it is copper depleting. It may deplete copper because of the high iron to copper ratio of most fruits.

There could easily be other dietary factors that affect the seasonal variation in hyperT symptoms. John

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MINERALS

This section now has information files on all minerals that have suspected function in the thyroid. Just click on the mineral names in hypertext in the left column. Some interesting ones: tungsten, strontium, gallium, indium, rubidium, and cesium.

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MITRAL VALVE PROLAPSE (MVP)

My feeling is that MVP is a condition caused by copper deficiency. Copper is essential for the formation of collagen which forms the structure of all the body. When copper gets deficient, MVP, Graves', hernias, gray hair, etc. result.

In the following study it is stated that " In contrast to early reports, true "MVP syndrome" as revealed by controlled studies consists of low body weight and blood pressure, minor skeletal abnormalities, orthostatic hypotension, palpitations, and mitral regurgitation that is usually mild." The symptoms of low body weight and palpitations sounds like the symptoms of copper (and iron) deficiency.
Curr Opin Cardiol 1995 Mar;10(2):107-16

Recent developments in the diagnosis and management of mitral valve prolapse.

Devereux RB

Division of Cardiology, New York Hospital-Cornell Medical Center, NY 10021, USA.

Mitral valve prolapse (MVP), which occurs in about 3% of adults, is usually a primary, dominantly inherited condition. MVP may be diagnosed by auscultation of a mid-systolic click and late-systolic murmur that move dynamically with postural maneuvers. M-mode echocardiography confirms MVP by demonstrating late-systolic prolapse and two-dimensional echocardiography reveals leaflet billowing into the left atrium. Echocardiography identifies severe forms of MVP by documenting significant mitral regurgitation, enlargement and thickening of the mitral leaflets and annulus, and loss of leaflet apposition. **In contrast to early reports, true "MVP syndrome" as revealed by controlled studies consists of low body weight and blood pressure, minor skeletal abnormalities, orthostatic hypotension, palpitations, and mitral regurgitation that is usually mild.** Complications of MVP include progressive mitral regurgitation, infective endocarditis, orthostatic syncope, and possible risks of neurologic ischemia and arrhythmic sudden death. Risk factors we have identified for complications among patients with MVP include older age, male gender, the presence of mitral regurgitation, and possibly, higher weight and blood pressure. The cumulative risk of all complications of MVP by age 75 is from 5% to 10% for affected men and 2% to 5% for affected women. Patients with MVP who have neither a murmur nor Doppler evidence of mitral regurgitation may be reassured that their condition is benign. For other patients with MVP we have shown that oral antibiotic prophylaxis is cost-effective. The presence and severity of mitral regurgitation govern the frequency and intensiveness of follow-up.

One of the dangers for people with MVP is bacterial endocarditis which is a bacteria infection of the heart. Bacteria which can cause this condition may enter the body through surface skin cuts or during dental or other operations. For this reason, antibiotics are prescribed before dental procedures. In the following article it is stated that "most cases of endocarditis are not attributable to an invasive procedure" but antibiotic pre-treatment is recommended for certain patients with MVP.

J Am Dent Assoc 1997 Aug;128(8):1142-51

Prevention of bacterial endocarditis: recommendations by the American Heart Association.

Dajani AS, Taubert KA, Wilson W, Bolger AF, Bayer A, Ferrieri P, Gewitz MH, Shulman ST, Nouri S, Newburger JW, Hutto C, Pallasch TJ, Gage TW, Levison ME, Peter G, Zuccaro G Jr

OBJECTIVE: To update recommendations issued by the American Heart Association last published in 1990 for the prevention of bacterial endocarditis in individuals at risk for this disease. **PARTICIPANTS:** An ad hoc writing group appointed by the American Heart Association for their expertise in endocarditis and treatment with liaison members representing the American Dental Association, the infectious Diseases Society of America, the American Academy of Pediatrics and the American Society for Gastrointestinal Endoscopy. **EVIDENCE:** The recommendations in this article reflect analyses of relevant literature regarding procedure-related endocarditis, in vitro susceptibility data of pathogens causing endocarditis, results of prophylactic studies in animal models of endocarditis and retrospective analyses of human endocarditis cases in terms of antibiotic prophylaxis usage patterns and apparent prophylaxis failures. MEDLINE database searches from 1936 through 1996 were done using root words endocarditis, bacteremia and antibiotic prophylaxis. Recommendations in this document fall into evidence level III of the U.S. Preventive Services Task Force categories of evidence. **CONSENSUS PROCESS:** The recommendations were formulated by the writing group after specific therapeutic regimens were discussed. The consensus statement was subsequently reviewed by outside experts not affiliated with the writing group and by the Science Advisory and Coordinating Committee of the American Heart Association. These guidelines are meant to aid practitioners but are not intended as the standard of care or as a substitute for clinical judgment. **CONCLUSIONS:** Major changes in the updated recommendations include the following: (1) **emphasis that most cases of endocarditis are not attributable to an invasive procedure;** (2) cardiac conditions are stratified into high-, moderate- and negligible-risk categories based on potential outcome if endocarditis develops; (3) procedures that may cause bacteremia and for which prophylaxis is recommended are more clearly specified; (4) an algorithm was developed to more clearly define when prophylaxis is recommended for patients with mitral

valve prolapse; (5) for oral or dental procedures the initial amoxicillin dose is reduced to 2 g, a follow-up antibiotic dose is no longer recommended, erythromycin is no longer recommended for penicillin-allergic individuals, but clindamycin and other alternatives are offered.

If you have any experiences with MVP or run across any info which might help others, please forward it to me for posting here. Thanks. John

Here is an interesting exchange from hyperthyroidism@egroups.com:

Subj: [hyperthyroidism] Re: Graves + Paxil + MVP
Date: 6/5/00 5:46:03 PM Pacific Daylight Time
From: tnccline@nemonet.com (Christine Cline)
Reply-to: hyperthyroidism@egroups.com
To: hyperthyroidism@egroups.com

--- In hyperthyroidism@egroups.com, KTenn36117@a... wrote:
Hello Deb,

It is interesting that I've noticed that a few people in the group who have thyroid problems ended up having mitral valve prolapse with mitral regurgitation. I was diagnostic as have MVP w/MR in January and February.

This was news to me. I really thought it might be inherited cuz my father had that and he had a mitral valve tear repaired about 3 years ago. Now it appears that one by one have come forward telling us that they were just recently having MVP along with Thyroid problems. I wondered if this is a big connection between thyroid and MVP???? What do you think??? John???
Kozy

Response from Christine:

Hi All!

Personally, I have yet to find a Graves' patient who HASN'T been diagnosed with Mitral Valve Prolapse, myself included.

The following is an excerpt from Dr. Walt Stoll, and it exposes the Mitral Valve Prolapse smokescreen for what it is:

"Mitral Valve Prolapse--the Current FAD Diagnosis (a diagnosis of convenience for the physician)

"The valvular condition described by this medical FAD is a harmless "normal variant" of the structure of the heart. The physician uses it as a blanket "explanation" for a myriad of symptoms the allopathic paradigm has no way of explaining separately. The physician says: "NOW we know what was causing all those symptoms you have had so long so we don't have to think about them anymore. Here take this pill for your MVP and go live with it."

"The Mitral Valve Prolapse (MVP) diagnosis is a current fad in medicine that has no clinical significance. Just because we CAN diagnose something doesn't mean it is important to that person's health. Unfortunately, putting a name to someone's symptoms does nothing about identifying the causes for them. One could have their MVP surgically corrected to normal and NONE of their symptoms, ascribed to the MVP, would change at all. As a matter of fact, this was actually done in the early days of this "diagnosis" and the fact that it did not change symptoms at all powerfully pushed the profession to their present stand that this is a normal variant of anatomy and is truly a non-symptomatic condition.

"Unfortunately, by the time the profession realized this, many physicians found how convenient it was to not have to face their multiply symptomated patient and admit that they had no idea what was causing their symptoms. Finally, they had some learned thing to tell the patient and it felt so GOOD that it is now very hard for them to let go of their "pacifier" and, once again, admit to the patient that they have no idea what is causing all their symptoms. SO, until the public becomes educated, they will continue taking medications for an imaginary condition."

So relax - it ain't so bad after all!!

Chris

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OSTEOPOROSIS

Br J Biomed Sci 1994 Sep;51(3):228-40

The role of nutrition in osteoporosis.

Bunker VW

School of Pharmacy and Biomedical Sciences, University of Portsmouth, England, UK.

Osteoporosis-related bone fractures are a significant cause of mortality and morbidity, with women being particularly affected. Osteoporosis is a condition of bone fragility resulting from micro-architectural deterioration and decreased bone mass; adult bone mass depends upon the peak attained and the rate of subsequent loss; each depends on the interaction of genetic, hormonal, environmental and nutritional factors. An adequate supply of calcium is essential to attain maximum bone mass, and adult intakes below about 500 mg/day may predispose to low bone mass. Supplementation with calcium may conserve bone at some skeletal sites, but whether this translates into reduced fracture rates is not clear. Chronically low intakes of vitamin D--and possibly magnesium, boron, fluoride and vitamins K, B12, B6 and folic acid (particularly if co-existing)--may pre-dispose to osteoporosis. Similarly, chronically high intakes of protein, sodium chloride, alcohol and caffeine may also adversely affect bone health. The typical Western diet (high in protein, salt and refined, processed foods) combined with an increasing sedentary lifestyle may contribute to the increasing incidence of osteoporosis in the elderly.

Drinking tea is associated with a higher bone mineral density in women even though high caffeine consumption is associated with osteoporosis. I believe the reason is the high levels of gallium compounds found in tea. Gallium is an extremely potent promoter of bone growth--see the gallium file for additional information.

Am J Clin Nutr 2000 Apr;71(4):1003-7

Tea drinking and bone mineral density in older women.

Hegarty VM, May HM, Khaw KT

Clinical Gerontology Unit, University of Cambridge School of Medicine, Addenbrooke's Hospital, Cambridge, United Kingdom.

BACKGROUND: High caffeine intake is reportedly a risk factor for reduced bone mineral density (BMD) in women. Most studies, however, are from populations in which coffee drinking predominates and is the major caffeine source. Tea contains caffeine but also has other nutrients, such as flavonoids, that may influence bone mass in different ways. **OBJECTIVE:** We examined the relation between tea drinking and BMD in older women in Britain, where tea drinking is common. **METHODS:** We measured BMD at the lumbar spine, femoral neck, greater trochanter, and Ward's triangle in 1256 free-living women aged 65-76 y in Cambridge, United Kingdom. Tea drinking was assessed by self-completed questionnaire and women were categorized as tea drinkers or non-tea drinkers. **RESULTS:** There were 1134 tea drinkers (90.3%) and 122 non-tea drinkers (9.7%). Compared with non-tea drinkers, tea drinkers had significantly greater (approximately 5%) mean BMD measurements, adjusted for age and body mass index, at the lumbar spine (0.033 g/cm(2); P = 0.03), greater trochanter (0.028 g/cm(2); P = 0.004), and Ward's triangle (0.025 g/cm(2); P = 0.02). Differences at the femoral neck (0.013 g/cm(2)) were not significant. These findings were independent of smoking status, use of hormone replacement therapy, coffee drinking, and whether milk was added to tea. **CONCLUSIONS:** Older women who drank tea had higher BMD measurements than did those who did not drink tea. Nutrients found in tea, such as flavonoids, may influence BMD. Tea drinking may protect against osteoporosis in older women.

PMID: 10731510, UI: 20197843

Ther Umsch 2000 Mar;57(3):152-60

[Osteoporosis diet].

[Article in German]

Morselli B, Neuenschwander B, Perrelet R, Lippuner K

Universitatsspital/Inselspital Bern.

Bone requires a wide variety of nutrients to develop normally and to maintain itself after growth. Most important--in the sense that bony abnormalities are associated with their deficiencies--are protein, calcium, phosphorus, vitamin D, C and K, zinc, manganese and copper. The nutrients most likely to be deficient in citizens of industrialized countries are calcium and vitamin D. In this review of the current literature about nutritional aspects of osteoporosis, we have focused on factors influencing calcium requirement: the principal interacting nutrients are sodium, protein, caffeine, fiber, oxalate, phytate, and the acid/alkaline ash character of the overall diet. Fiber and caffeine decrease calcium absorption from the gut and typically exert relatively minor effects, while sodium, protein and the acid/alkaline balance of the diet increase urinary excretion of

calcium and are of much greater significance for the calcium homeostasis. Alkali buffers, whether vegetables or fruits reverse this urinary calcium loss. As long as accompanied by adequate calcium intake, protein-rich diet is not deleterious to bone: a calcium-to-protein ratio of 20:1 (mg calcium/g protein) is recommended. Whether a nutrition-based therapeutic approach to osteoporosis is feasible in the near future is yet unclear: at least there are some recent promising data from in-vitro as well as from rat studies showing that extracts taken from various vegetables, mainly from the onion family inhibit bone resorption in a dose-dependent manner.

The following study shows that cadmium interferes with calcium metabolism and may therefore be a contributor to osteoporosis. This is very likely the mechanism by which smokers, especially female smokers (from estrogen acceleration of cadmium uptake) develop osteoporosis.

Biomed Environ Sci 2000 Mar;13(1):19-25

Changes in tissue metals after cadmium intoxication and intervention with chlorpromazine in male rats.

Yang XF, Wang SY, Zhao RC, Ao SQ, Xu LC, Wang XR

Institute of Applied Toxicology, Nanjing Medical University, China. xfyang@njmu.edu.cn

[Medline record in process]

Cadmium (Cd), one of the most dangerous heavy metals, has a very similar ionic radius to calcium (Ca). The interference of cadmium in calcium homeostasis may play an important role in cadmium toxicity. Recent reports indicate that calmodulin (CaM) inhibitors such as trifluoperazine and chlorpromazine (CPZ) could protect rodents against cadmium toxicity. It was also reported that pretreatment of mice with zinc (Zn) could reduce the adverse effects induced by cadmium. The aim of this study is to determine whether Cd changes the balance of other essential metals such as Zn and copper (Cu) in rat tissues, and whether CPZ can reverse these changes which are induced by cadmium intoxication. Adult male Sprague-Dawley (SD) rats were injected intraperitoneally (i.p.) with cadmium chloride (CdCl₂) (0.2, 0.4, 0.8 mg Cd/kg body weight) alone and 0.4 mg Cd/kg in association with CPZ (5 mg/kg) daily for a week. The control animals were injected with normal saline only. The results showed that the cadmium content in the liver, kidney and testis increased significantly with a dose-response relationship. Cadmium treatment markedly increased the Zn and Ca content in some of the tissues. Hepatic and renal metallothionein (MT) increased significantly after cadmium intoxication. CPZ treatment, however, reduced cadmium content in liver, but not blood and kidney. CPZ seemed to decrease the content of MT in liver and significantly increase the amounts of MT in kidney. These data suggest that the intervention of cadmium with tissue essential metals may play a role in cadmium toxicity in rats, and calmodulin inhibitors to some extent can reduce the adverse effect of cadmium by decreasing the cadmium load in tissues and reversing the unbalance of essential metals.

The following study shows that vanadium supplementation can increase bone mineral levels and that there is an interaction between vanadium and vitamin C in cholesterol metabolism.

Magnes Trace Elem 1991-92;10(5-6):327-38

Vanadium and ascorbate effects on 3-hydroxy-3-methylglutaryl coenzyme A reductase, cholesterol and tissue minerals in guinea pigs fed low-chromium diets.

Seaborn CD, Mitchell ED, Stoecker BJ

Department of Nutritional Sciences, Oklahoma State University, Stillwater.

Vanadium has been reported to affect numerous physiological processes; however, a demonstration that vanadium deficiency consistently impairs biological function is lacking. The purpose of this study was to determine if the activity of hepatic 3-hydroxy-3-methylglutaryl coenzyme A (HMG CoA) reductase, the rate-limiting enzyme in cholesterol synthesis, is affected by dietary supplementation of vanadate and/or chronic ascorbic acid deficiency. To determine if vanadium and/or ascorbic acid affected mineral metabolism, tissue minerals also were analyzed. Weanling male guinea pigs were assigned randomly to groups of 10 in a 2 x 2 factorial design. The dietary variables were ascorbate, 0.5 or 10 mg/day, and vanadium < 0.01 microgram or 0.5 microgram/g diet as NH₄VO₃ in a low Cr diet containing < 0.07 microgram Cr/g diet. After 21 weeks on this diet, guinea pigs receiving more ascorbate had lower liver weight/body weight ratios and increased bone copper. Testes weight/body weight ratios, hepatic glycogen and bone copper decreased while hepatic lipids, fecal bile acids, plasma cortisol and bone calcium and magnesium were increased by vanadium supplementation. An interaction between vanadium and ascorbate affected cholesterol excretion in feces, hepatic iron, plasma cholesterol concentration and the activity of HMG CoA reductase. **This study provides evidence of increased bone mineral concentrations with vanadium supplementation and of an interaction between vanadium and ascorbate which affected cholesterol metabolism.**

June 15, 2000

CHICAGO (AP) - Teen-age girls who drink soda - particularly cola - are far more likely to break a bone, a Harvard study found.

Grace Wyshak, an associate professor at the Harvard School of Public Health and Harvard Medical School, speculated that girls drinking soda aren't getting enough milk, which contains calcium that strengthens bones.

But she also suggested that a chemical in colas - phosphoric acid - may actually weaken bones.

The study, published in this month's Archives of Pediatrics & Adolescent Medicine, was based on questionnaires filled out by 460 ninth- and 10th-grade girls in a Boston-area high school.

The risk of broken bones was three times greater for girls who drank carbonated beverages in general and five times greater for active girls who drank colas. The study did not specify how much soda the girls drank.

Five of the 57 active girls who didn't drink colas suffered fractures, compared with 38 of the 107 active girls who reported drinking colas.

A spokesman for the National Soft Drink Association, Sean McBride, said: "We strongly question the results of the journal article." He said there is no scientific evidence that anything in colas causes fractures.

The study comes amid growing concern among experts, who say Americans are not getting nearly as much calcium as they need, in part because they are drinking soft drinks instead of milk.

"This should be a wake-up call for parents and health care professionals alike," said Bonnie Liebman, director of nutrition at the Center For Science in the Public Interest, a consumer advocacy group.

In an accompanying editorial, Dr. Neville H. Golden, director of the Eating Disorders Center in the Division of Adolescent Medicine at Schneider Children's Hospital in New Hyde Park, N.Y., said the study suggests that "osteoporosis is a pediatric disease as opposed to a disease of older people and that we can have some impact on it early."

In a previous study, Wyshak found increased bone fractures among adult women who drank carbonated beverages.

Stronger Bones, More Breast Cancer?

□

June 19, 2001

*By Lisa Ellis
InteliHealth News Service*

Elderly women with strong bones are less likely to break them, but it appears they may face a different risk — breast cancer.

A study published in the June 20, 2001, issue of the Journal of the National Cancer Institute adds to a volume of evidence that postmenopausal women with low bone-mineral density — the "brittle bones" disease called osteoporosis — are less likely to get breast cancer, but women with healthy bones may be at least twice as likely to do so.

The research points to one of the paradoxes of women's health care — that risk factors for some diseases may be protective against others. Moderate alcohol consumption, for instance, can provide some protection against heart disease in women after menopause, but it simultaneously may increase their breast-cancer risk.

What does the research on bone-mineral density mean for women trying to protect their health?

"It's not clear what the real implication of this is for most patients," says Harold Burstein, M.D., Ph.D., an instructor in medicine at Harvard Medical School and a breast-cancer researcher at Dana-Farber Cancer Institute.

He says the increased risk is relatively small. "Most older women do not get breast cancer," he notes. "While the data show an association between bone mineral density and breast cancer risk, it is by no means clear that changing bone mineral density — up or down — changes that risk."

Indeed, the study's authors caution that the association between bone density and breast cancer does not mean that strong bones cause cancer or that women should stop trying to maintain bone mass through taking calcium or medications.

Rather, the cancer and the bone-mineral density both are likely to be related to a long-term, complex relationship

among hormones and certain other body chemicals, the authors say.

Many researchers believe the chief cause may be "a shared risk factor, lifetime exposure to estrogen," Dr. Burstein says. Osteoporosis, a thinning of the bones that can lead to fractures, tends to develop after menopause, when women's estrogen production drops. Breast-cancer risk is higher among women who have greater lifetime exposure to estrogen, including early menstruation and late menopause.

Some women take estrogen supplements after menopause to ease the symptoms of this life change or to help protect against osteoporosis. But there are many other means of preventing or treating osteoporosis that do not involve estrogen, Dr. Burstein says.

Calcium and Vitamin D supplements, weight-bearing exercise and quitting smoking all reduce the risk of osteoporosis, and certain medications can help to slow the rate of bone loss, he says.

The study published in the Journal of the National Cancer Institute enrolled more than 8,900 women, ages 65 and older, who were examined at medical centers in Pittsburgh, Minneapolis, Baltimore and Portland, Ore., between 1986 and 1988. During an average of 6.5 years of follow-up, 315 women developed breast cancer.

Those who had the highest bone-mineral density, a measure of bone mass or thickness, at all three sites measured — the wrist, arm and heel — were 2.7 times more likely to develop breast cancer than those who had the lowest bone-mineral density at all sites.

What is more, the women with the highest bone-mineral density were even more likely to get advanced cancer — 5.6 times more likely than the women with the most brittle bones.

The relationship between bone-mineral density and breast-cancer risk is well established at this point, Dr. Burstein says.

"The novel finding (in the new study) is that women who have higher bone mass seem to have a more advanced tumor stage, so it seems to increase your risk of having a slightly more advanced breast cancer," Dr. Burstein says.

But he noted that only 74 of the 315 women who developed cancer had these more advanced tumors. He says larger studies would be needed to prove that women with stronger bones have higher risk not only for breast cancer, but also for more invasive forms of the cancer.

The multi-center study, which used data from the long-term Study of Osteoporotic Fractures, reinforces similar results from a shorter-term study involving the same group of participants and a much smaller study of about 1,300 women in Framingham, Mass. Other studies have found that women who have bone fractures are less likely to get breast cancer.

Researchers in the current study found that the association between high bone density and breast cancer persisted even when they allowed for certain factors that are associated with a greater chance of breast cancer — obesity, use of estrogen supplements, and record of fewer screening mammograms.

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OVERWEIGHT

INTRODUCTION

I've listed being overweight under disease conditions even though it's not normally thought of as a disease. However, I consider being overweight, especially when it's associated with thyroid disease, as a disease condition. It is very often an abnormal health condition which is the result of nutritional deficiencies.

Before getting into the discussion of weight control, however, I'd like to preface it with a warning. Current fashions have set the ideal body weight at an extremely low value. In prior years a woman who was 5'4" tall was considered attractive if her weight were 20 pounds more than what is considered ideal today. Today the emaciated look is considered stylish, but I don't think that being extremely thin is best for health. I think a person's first goal is to get healthy even if that means not being extremely thin. You should try to get to a weight where you maximize energy, vitality, and strength and be happy with that weight whatever it is. Some people, because of body build and genetics, are going to be heavier or lighter than others. Find the optimum weight for you and don't get obsessed with attaining an unhealthy thinness.

The important factor concerning body weight is that it is a measure of your overall health. Being underweight or overweight is an indication that something is wrong with your health. Body weight is an observable measure of your health which you can use to determine if you are making progress.

There are a lot of nutritional and activity factors that affect weight. Many of these factors control the body's rate of metabolism, or how fast energy is produced from the food eaten. A person with a fast rate of metabolism uses calories up fast and is generally thin, while a person with a slow rate of metabolism is more likely to process food into fat. Exercise is known to raise the rate of metabolism for a period of time afterward (6-8 hours), so that a person will burn more calories in the hours after exercise as well as during exercise. In addition there are many nutrient factors that regulate the rate of metabolism. Before we get into those factors, let's look at what determines the rate of metabolism.

THYROID EFFECT ON WEIGHT

The thyroid controls the rate of metabolism in the body. How fast energy is produced in the body's cells is directly proportional to the T3 (triiodothyronine) that gets to those cells. If the thyroid is not producing sufficient hormone or the T4 hormone that the thyroid gland is producing is not being converted to enough T3 for the cells to use, or the cells are not receptive to the actions of T3, then the rate of metabolism will be low. A low metabolic rate is the main reason for being overweight.

A person with low thyroid function can exercise an hour or more a day, eat 1500 calories or less a day, and still gain weight. A person with high thyroidal function as seen in hyperthyroidism will lose weight including muscle mass even if they don't exercise and eat 3000-5000 calories a day. The lesson here is that thyroidal function is the most important variable in controlling weight. Exercise and caloric intake are factors, but are very small factors compared to the effect of thyroid hormone.

There are people who take thyroid hormone such as Synthroid for the sole purpose of keeping their weight down. This is not a good idea since it doesn't correct the underlying nutritional deficiencies which are causing the weight gain. Our thyroid glands have tremendous capacity to increase and decrease production of thyroid hormone as our bodies need changes. Getting our thyroid to produce the right amount of hormone naturally is much preferable to having to constantly monitor and adjust the amounts of an ingested hormone supplement. Let's look at how to increase thyroid output so that our bodies don't accumulate fat.

STEP ONE: DON'T FAST OR RESTRICT CALORIES

Most people know the lesson of how dieting affects metabolic rate but it's worth repeating. Restricting caloric intake causes the thyroid to reduce production of thyroid hormones and thereby lower the metabolic rate. This is an innate mechanism which has the result of preserving life when food is scarce. By eating less you lower your rate of metabolism and when you resume eating you gain weight rapidly.

Fasting and caloric reduction interspersed with periods of eating freely are the very best ways to gain weight and this technique is recommended for underweight persons. The problem is that this causes the thyroidal function to remain depressed, with consequent low energy levels, until the proper cues cause the thyroid to resume normal output. The lesson here is that if you want to lose weight don't do things to convince your body that there is a famine so that it reduces the metabolic rate to preserve body fat.

STEP TWO: CONVINCE YOUR BODY THAT FOOD IS ADEQUATE

Our bodies use many cues in determining how to set the body's thermostat, the thyroid. If protein or fat are restricted, the body senses that food is scarce and lowers the thyroidal output. If you consciously lower your protein and fat intake you will consume more calories than necessary because you'll have to eat more carbohydrates to make up the needed calories. Eating carbohydrates to the exclusion of fats and proteins causes you to overeat in order to get all the protein and fat that your body requires. Eat adequate amounts of protein and fat to satisfy your body's needs most efficiently without requiring it to sift through vast amounts

of food to get these nutrients.

If protein and fat get severely restricted, thyroid output increases to the point where hyperthyroidism results. This is basically the body's last gasp to give you enough energy to go out and find some food to prevent death. Nutrients are severely depleted and the body begins to consume its own tissues for needed nutrients. Hyperthyroidism causes weight loss but this is not a good way to lose weight. It greatly increases long term nutrient deficiencies which take a long time to completely correct.

STEP THREE: GET ALL THE NUTRIENTS YOU REQUIRE TO AVOID NEEDING TO OVEREAT.

We crave food to satisfy our needs for all the essential nutrients. Besides essential amino acids in proteins and essential fats, we need minerals and vitamins. By eating foods which are deficient in nutrients, we need to eat an excessive amount of food to obtain all the essential nutrients. This is the reason eating white flour products and white sugar products causes weight gain--the lack of nutrients requires us to eat more of other foods to make up for the deficient nutrients.

Some of the foods that we eat will be deficient in key nutrients, usually minerals, because the soil on which they were grown was deficient. Eating a wide variety of foods and taking mineral supplements is the best way to avoid overeating in order to obtain all the necessary nutrients.

One of the ways that exercise helps us to lose weight is that it burns up calories allowing us to eat more food. With this increase in food intake, we take in more nutrients and are more likely to get the nutrients that we need.

This same principle applies when we are gaining weight. We are eating more food so we are getting more nutrients. The opposite happens when we try to eat less to lose weight: we become deficient in nutrients because of the reduced food intake. This is one reason why taking nutritional supplements helps lose weight: we don't need to eat a huge amount of food to obtain the required nutrients.

STEP FOUR: TRUST AND FOLLOW YOUR CRAVINGS

A food binge is an uncontrollable need to eat a particular food or class of foods. Our body's primitive brain which is wired for survival takes over because the thinking brain has made decisions which have led to a nutrient deficiency. While a food binge is a failure of will power, it's in the interest of the body to overpower the will.

Some people have extremely strong will power and can resist any food temptation. They develop an eating plan based upon their own or other's ideas and rarely give in to their temptations. They are completely subverting the body's innate mechanisms to obtain needed nutrients and they usually pay with increasingly poor health. I've been one of these people and seen lots of these people. You get sicker and sicker and wind up with many "food allergies" and chemical sensitivities which eventually cripple your life. Eventually you'll probably get hyperthyroidism or another endocrine disease. Trust your body to tell you what to eat.

If you have food binges, then it's important to find out what this indicates about your deficiencies. Sometimes by studying the foods you crave you can determine what nutrients you are missing. Sometimes the nutrients are obscure trace elements and you may never figure it out. However, if you can figure out what nutrients, which are usually minerals, that you are craving, you can supplement these and thereby reduce the need to eat huge amounts of the food which contains them.

Binging usually scares people because their eating feels completely out of control. To regain control, people put themselves "in jail", i.e. they go on a diet. However, if this diet does not contain all the needed nutrients, sooner or later there will be a "jail-break" and the person will go on another binge. This cycle of dieting and binging is very deleterious to the health and usually has the long-term effect of an increase in fat retention because the body interprets this as a famine-and-feast situation. It is much better to eat the foods you crave so that the nutrients you need don't get severely deficient.

NUTRIENTS WHICH CONTROL WEIGHT

Now that we have a general idea of what to do and what not to do so that our body doesn't "intentionally" slow thyroid function, let's look at the nutrients which affect thyroid function and thereby control the rate of metabolism. First, however, let's look at one factor which is difficult to call a nutrient but which affects nutrients.

RAW FOODS

If you ever really need to lose weight there is one sure method: eating raw foods. I ate raw foods for a whole year when I was younger and know many people who have done this for varying lengths of time. I know one person who has eaten an exclusively raw diet for about 30 years. He is about 65 years old but looks about 45 years old. In his description, he is "free from disease."

If you want to lose weight and have a tremendous increase in energy, it's possible to do this by eating an all-raw diet. However, there are some rules which you have to follow. The most important and hardest to follow is to restrict fruit consumption. My friend says the general rule is to eat two vegetable meals for each fruit meal. It is very easy and tempting to eat just fruit and you can eat a tremendous amount of fruit and not

gain weight. However, eating only fruit depletes you of certain nutrients such as copper and zinc and in the long term you'll get sicker and sicker. Your energy level will drop and you will get thinner and thinner. There is a name for this and it's called malnutrition. Vegetables including ones we don't normally eat raw like squash and pumpkins are important to get all the necessary nutrients.

Eating raw foods will cause you to lose weight. You can eat all you want of any food as long as it's raw and not get overweight. If you ate only raw foods and became overweight it would be somewhat of a miracle.

If you have hyperthyroidism I would definitely not recommend starting a raw food diet. I've tried this and it just makes things worse. It's possible that starting an all-raw diet while hypo may not be a good idea either. The problem is that hypos are usually deficient in zinc and zinc is a difficult mineral to get on a raw food diet. Seeds like sunflower and pumpkin are good zinc sources, but in general zinc is scarce in a vegetarian diet. Selenium is important for hypos and selenium is actually more available in raw foods than in cooked foods. Cooking makes selenium less available for some reason. I wouldn't recommend to anyone who has a thyroid disease to start a raw food diet without a guide, someone who has done it and who can show you the way.

The important message about raw foods for those who wish to lose weight is that raw foods increase the rate of metabolism and will not cause weight gain. The foods that cause weight gain are cooked foods. Eat as high a percentage of raw foods that you are comfortable with and try to gradually increase that percentage.

If you are overweight and hypo remember that fruits are good for losing weight. The sugar in fruits will not cause you to gain weight. You can eat 10 pounds of fruit a day and not gain weight. I know because I've done it and known others who have done it. I don't recommend eating this much but just don't avoid fruit because you believe the sugar will make you gain weight. Cooked sugar will probably cause you to gain weight but not raw sugars in fruits.

Raw nuts and seeds are an excellent way to get raw proteins, fats, and minerals. These foods contain every nutrient necessary for life because they will grow into a plant. Eat raw nuts and seeds every day and use them to get your fat instead of eating cooked fat.

So if you are trying to lose weight, consider all raw foods to be "free" meaning that you can eat all you want of them. You only have to be careful about overeating cooked foods. For example if you are craving potatoes, eat raw potatoes (peeled--don't eat the skin) instead of cooked potatoes. At the end of the day when you are wired from eating raw foods all day, you may crave some cooked foods to help you relax.

Start each day as if it were going to be an all-raw food day. Try to go as long as possible. You'll find that raw foods will add to your energy level and get you through the day much easier than eating cooked foods, which have half their vitamins destroyed. At night or when you crave cooked foods, eat them. If you crave a hamburger or a pizza, go for it. Remember, don't deprive yourself of eating the foods you crave. Just try to postpone the cravings to the end of the day so that you have a good chance of satisfying those nutrient needs with raw foods first. Don't go to sleep without getting your day's food (remember nutrient) cravings satisfied.

SUPPLEMENTS FOR WEIGHT LOSS

The supplements which increase weight loss are basically the same ones which are recommended to increase thyroid function for hypos. Nutrients can be divided into two classes: those that increase thyroidal function and those that decrease it. To lose weight it's important to know which ones are which and what foods contain these nutrients. Before we get into specific nutrients, however, let's look at what may be the most important factor: digestive enzymes.

DIGESTIVE ENZYMES

People who have thyroid disease and those who are overweight probably have poor digestion. This seems counterintuitive because you would think that people who are overweight have very good digestion, perhaps too good. However, the problem which causes overweight does not seem to be the amount of food which is converted into calories. Rather it is thyroidal function which determines the rate of metabolism and thereby determines the body weight.

What nutrients get into your cells is dependent on two things: what you eat and what portion of what you eat gets digested so that it can be assimilated. The key to assimilation is digestive enzymes. Without digestive enzymes, your food cannot be broken down and assimilated. There are many specific digestive enzymes that our bodies produce and these digest different types of foods such as carbohydrates, proteins, and fats. It's possible to have some digestive enzymes and not others so that you can easily digest carbohydrates but can't digest fats or proteins well.

Additionally, these digestive enzymes require trace elements for their manufacture in the body. Once you get deficient in a trace mineral required for a digestive enzyme, the digestive enzyme is not made in sufficient quantities. Your digestion decreases and then your supply of trace elements, fats, and proteins also decreases. This leads to the classic vicious circle where your health condition continually deteriorates. The best way to break this cycle is by taking digestive enzymes until the nutrients are replenished and your body is able once again to manufacture its own digestive enzymes.

People who are overweight because of low thyroid function are probably deficient in trace minerals and this

deficiency could be from a lack of ingestion of foods which contain the trace minerals or it could be from the body's inability to extract the trace minerals from the food. I suspect that the latter condition is more prevalent.

What probably happens is that the person is able to digest the simple carbohydrates, i.e. the starches and sugars, well and these are converted into fat because of low thyroid function. What isn't being digested well are the proteins, fats, and complex carbohydrates which contain the essential trace minerals. The result is lowered muscle mass from lack of protein and the breakdown of energy producing systems in the body leading to lower energy levels. Eventually you also develop trace mineral deficiencies which hamper thyroidal function and cause the food to be converted to fat.

When I was really hyperthyroid, I started taking digestive enzymes and noticed that my thyroidal function increased resulting in more severe hyper symptoms. Eventually I tracked it down to this: the digestive enzymes only made me more hyper when I also took a zinc supplement. My body was not digesting and absorbing zinc well on its own, and the digestive enzyme greatly increased the bioavailability of zinc.

Hypos are usually zinc deficient and this deficiency is an important cause of their hypothyroidism and weight gain. Zinc seems to be particularly hard to assimilate in persons with digestive deficiencies. This is the reason why hypos and those who are overweight should take digestive enzymes: to increase zinc absorption, because zinc is a key mineral for increasing thyroidal function.

CALCIUM

Calcium has recently been found to play a role in weight control. A study on mice found that "How much calcium the animals consumed-and its source-greatly affected what share of their meals turned to fat. Reanalysis of data collected earlier on women supports that finding, another scientist adds."

Interestingly, calcium is also involved in thyroid hormone metabolism. One study on the effect of calcium on thyroid metabolism states: "The present study provides conclusive evidence for two central issues: that calcium is the first messenger for the prompt, plasma membrane-mediated action of thyroid hormone to increase cellular sugar uptake, and that thyroid hormone produces an acute increase in calcium uptake by the heart, an effect that is demonstrable at physiological concentrations and is thyroid hormone specific and, therefore, points to a physiological relevance for this action." **Calcium is considered the first messenger of thyroid hormone at the plasma membrane. What this means is that if calcium is deficient, the thyroid hormone will not have the full effect on the cells in increasing the cellular metabolic rate.**

In our research we've seen that hypers have to restrict calcium and supplement magnesium (the opposite mineral to calcium) to reduce the impact of the high thyroid hormones. Generally hypers need more magnesium and hypos need more calcium. Now we see that by increasing calcium, it's possible to lose weight because of the effect of calcium on increasing the cellular response to thyroid hormone and the resultant increase in metabolic rate.

You can read the full story from Science News by clicking here: [Calcium may become a dieter's best friend](#)

ZINC

Zinc, selenium, iron, manganese, and chromium may be the most important minerals to regulate body fat because of their important roles in thyroid hormone metabolism.

CHROMIUM

The following study shows that a weight gain will result if copper is adequate and chromium is deficient.

Sci Total Environ 2000 Apr 17;249(1-3):133-42

Experimental copper and chromium deficiency and additional molybdenum supplementation in goats. I. Feed consumption and weight development.

Frank A, Anke M, Danielsson R

Department of Clinical Chemistry, Faculty of Veterinary Medicine, Swedish University of Agricultural Sciences, Uppsala. dr.a.frank@rocketmail.com

Secondary Cu deficiency, Cr deficiency and molybdenosis were suggested causes of the 'mysterious' disease afflicting moose (*Alces alces* L.) in a region in south-west Sweden affected by acid rain. A model experiment with goats was performed to study the clinical chemical parameters, determine the tissue contents of trace and minor elements, to perform pathological and histopathological investigations and to compare the findings with those in moose disease. Twenty 3-month-old male goats were assigned to four dietary treatments (five animals each) in an experiment lasting for 20 months. The four groups in the study were: control group, Cu-deficient group (group 1), Cr-deficient group (group 2), and Cu- and Cr-deficient group (group 3). The animals were fed a basic semi-synthetic diet. At the end of the study the three surviving animals of group 3 were supplemented with additional tetrathiomolybdate (TTM) during the last 2 months. Feed consumption and

weight development of the animals were monitored and are presented. The feed consumption of the two Cu-deficient groups of goats (group 1 and group 3) supported the previously described observations in copper deficiency in ruminants, e.g. decreased appetite and feed intake. A previously unreported effect of Cr deficiency in ruminants is now described in goats. **Chromium deficiency at adequate Cu supplementation (group 2), caused increased lipid synthesis and a weight gain of 32 kg compared with that of the control group (20 kg).** A possible explanation for this unexpected weight increase in only Cr deficiency is discussed. It is concluded that the feeding experiment does not support the hypothesis concerning the relation of Cr deficiency to the moose disease.

John... please address weight loss

February 26, 2002

From: Lisa D.

T1: blader5658@aol.com

Comments

John, I have avidly read every bit of info on your site here and I thank you for your dedication. I have been hypo for about 9 years now. At onset I went from being very thin to twenty five pounds heavier. After two years of not knowing what was wrong I was diagnosed and RX'd Synthroid. I immediately lost 20 pounds. I maintained that for quite a while but as time progressed I began gaining and gaining no matter how little I ate or what I ate (low carb, no carb, low fat, liquid, etc.) or how hard or how much I exercised. So now I am on 2 gr. Armour and on a low carb eating regimen, but I am still about 35-40 pounds overweight. I began your supplement recommendation - I was already taking many of the things you suggest but what I really want to know is if you know of hard evidence that these supplements help hypos lose weight. I know you seem to be more focused on hyper which I understand as it is life threatening but I would really like you to address this if you could. It may seem like it's not as important as other issues but it profoundly affects every minute of my life - I feel like I'm in a strange body. Thank you again for your hard work and for your time in answering this question.

Hi Lisa,

I know that a lot of people have problems being or feeling overweight. Before we get to the weight loss part, however, I'd like to say that I feel that being healthy is the first step and needs to be placed before weight loss.

If you make sure that you are getting all your nutritional needs and your energy is high, then I believe that the resulting impact on your life will be to be busier, exercise more, and to have a higher rate of metabolism.

Also, I feel that many people who look thin may not be healthy. The anemic, amphetamine-abusing look is in, but that doesn't mean it's good for you. Most people will probably feel better and be healthier if they are 5-15 pounds over what they believe to be their "ideal" weight.

However, if you are really overweight and you once were thinner, then it should be possible to get back there. We know how to stimulate the thyroid to increase thyroid hormone production and thyroid metabolism is the most important thing in weight control. A hyper can eat 5000 calories, not exercise, and lose weight; while a hypo can eat 1000 calories, exercise for hours, and gain weight. Hypos can actually gain weight on water, because the sodium/potassium balance is out of whack allowing the body to gain water weight (edema).

To stimulate the thyroid, we can do the opposite of what helps hypers. Hypers need copper and less zinc, so to lose weight we can increase zinc and decrease copper. Hypos might experiment with high amounts of zinc to see what happens--perhaps 50-100 mgs.

Hypers need more magnesium, so hypos need to increase calcium. Most cal/mag supplements are a 2:1 ratio (cal:mag). Hypers need to get the ratio toward or beyond 1:1. Hypos might need a higher ratio (3:1, 4:1, etc.) More calcium has been shown to promote weight loss in studies and gives the muscles more power, increasing athletic performance.

Many of the B vitamins push copper metabolism, like biotin, PABA, B1, B2, B3, B5. A hypo might want to take more B6, folic acid, and B12. These three B's will stimulate the thyroid. B6 in particular pushes zinc metabolism.

Iron metabolism is also important. Extra iron gives strength to the muscles and allows excess copper to be utilized. This lowering of excess copper will increase thyroid production.

Potassium is very important. While it's important to get adequate protein, you can't eat an all-protein diet. You need carbs and high potassium foods. Potassium is the key mineral that prevents the condition of edema where water fills the cells causing your whole body to swell. You can check edema by looking at your sock line after hours of wearing socks. If the sock area is indented compared to the area above, then you have edema and need more potassium. Potatoes, bananas, tomato juice, and vegetables are all good potassium sources. Taking supplements can help, but remember that we need 3000 mgs of potassium daily. If you take 10 potassium tablets, this is only one third of the daily requirement. However, taking 10-15 potassium tabs a day can add to your ability to meet your

requirement. In order to replenish a body which is depleted of potassium, it might take 4000 mgs a day. Remember that food is the best way to get potassium and use supplements only as an addition.

I believe that zinc is the key metal which pushes potassium metabolism. If you have edema and potassium isn't doing much, you may need extra zinc to make the potassium work better. Also, there are probably some B vitamins that help potassium. I'm not sure which, but B5 might be the most likely.

Stimulants can have the opposite effect for those who need to lose weight. For example, tea (green and black) has high levels of fluoride. Fluoride is an iodine antagonist and therefore decreases thyroid hormone production. Tea is great for hypers, but not for hypos. It can cause weight gain for some. Losing weight by taking stimulants is not only a bad idea for your health, it may backfire.

The most important thing is to develop a supplement program which will stimulate the metabolism, without going over the edge (becoming hyper). Know the warning signs of hyperthyroidism: elevated heart rate, heart rate that doesn't return to normal soon after exercising, feeling hot and sweaty, shaking, etc. Make sure you don't go hyper.

If you have the right supplement program, you'll have incredible energy, want to exercise for hours, and be excited about everything, including work. Once you are at this point you'll have the energy to get into great physical shape. If you're in good physical shape and have enough endurance to run 10 miles, then you're going to lose weight. If you're doing the equivalent of a 6-10 mile run 4-5 times a week, there is no way you can be overweight. You just need to find a form of exercise you can do that doesn't hurt your body.

I've found that my body weight will go up 15-20 pounds (about 10% of my body weight) if I stop exercising for a few weeks. This is normal. So make sure you maintain a vigorous exercise program to keep your weight down that last 10%.

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PARA-AMINOBENZOIC ACID (PABA)

PABA is one of the B vitamins that helps copper metabolism.

From: Darlene

T1: Dittomom1@aol.com

Remote User:

Comments

Started supplementing PABA about two years ago, on a blurb in "Prescription for Nutritional Healing" by James and Phyllis Balch. "Delays wrinkles." Bought some.

I'm 43, and just starting to gray. Dark brown hair, so they're really noticeable. My secret to younger looking hair? The needle-nosed pliers. Works great. My point in saying that, is that because I yank them individually, I have a good feel for how many there were last time, and if there are more, etc. Before I went hyper, I got lazy once, and didn't replace the PABA when I ran out. It was supposed to delay wrinkles, but I hadn't read that anywhere else, so, what's the big deal? I swear, the grays sprouted like weeds. So I yanked them again, replaced the bottle, and now they're coming in a more "manageable" pace.

The most interesting event though, is that I hadn't noticed my graying when I first started the PABA. Then when I started pulling them, I'd look closely to make sure I'd "bagged" the correct hair (takes practice). About six months into it, on at least three occasions, I remember looking at a hair that was obviously gray on the oldest part, abruptly changed back to dark brown, and continued to dark brown into the newest, "follicle" part. Couldn't have mistaken, either, as the "new" end has a round sphere-like thing on the end of it. Even showed it to my mom, as it was so bizarre (if anything, it's supposed to do the opposite).

I strongly believe it was the PABA. Won't do it on all the follicles, but if you're determined not to "cover the gray" chemically, you may be doing two good things with one supplement I was taking about 200 mg./day. I'm at 300 now.

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PARKINSON'S DISEASE

Study Links Pesticides, Parkinson's

November 6, 2000

The Associated Press

New research using rats suggests that long-term exposure to a widely used pesticide kills brain cells and triggers debilitating physical symptoms associated with Parkinson's disease.

Scientists say the experiment's results strongly indicate what scientists have suspected for several years - that the most common form of Parkinson's disease might result from toxins in the environment.

The new study, published in the December issue of *Nature Neuroscience*, does not prove that the pesticide used in the test, rotenone, causes Parkinson's in humans.

But scientists who reviewed the experiment said the results are powerful and should reinvigorate the search for environmental toxins that may contribute to Parkinson's, the most common neurological disorder after Alzheimer's.

"This is more evidence that a class of compounds may increase the risk of developing Parkinson's," said J. William Langston, director of the Parkinson's Institute in Sunnyvale, Ca., who was not involved in the study. "It is not direct evidence that rotenone causes Parkinson's. The whole puzzle hasn't come together."

More than one million Americans suffer from Parkinson's. Muscle control ebbs as brain cells in a region called the substantia nigra produce less dopamine, a hormone vital to normal nerve function. The illness is marked by small tremors, such as facial tics and shaking hands. Advanced symptoms include a shuffling gait, speech difficulties and muscle weakness.

There is no cure, and current drug and surgical therapies tends to lose effectiveness over time. New therapies involving transplants of stem cells, the body's master cells from which all tissues grow, have been slowed by federal funding restrictions on experiments using embryonic tissues.

In about 10 percent of patients, Parkinson's strikes before age 50. These rare cases probably are caused by inherited genetic abnormalities.

However, most patients show their first Parkinson's symptoms after age 60. Researchers believe older patients may have suffered brain damage from chronic exposure to unspecified toxins. Among the suspects: pesticides, industrial chemicals and tobacco smoke.

In the experiment conducted at Emory University in Atlanta, neurologists implanted tiny pumps in the rats to continuously administer low doses of rotenone through the jugular vein for as long as five weeks.

Rotenone is an organic product made from extracts of tropical plants. It is widely used as an agricultural pesticide and to kill unwanted fish in reservoirs.

People most frequently would be exposed to rotenone by ingesting residue in food or by handling the compound.

Scientists acknowledged the pump method used in the experiment did not duplicate rotenone exposure in the real world, but said it was a more direct and reliable method for research purposes.

"Rats can be picky about what they eat and they might not like eating rotenone," said J. Timothy Greenamyre, the study's senior author. "Whether the pesticide would have the same effect in people via normal routes of exposure is not clear."

Greenamyre said half of the rats gradually showed Parkinson's symptoms.

Examination revealed that large numbers of dopamine-producing cells in the rats' brains had died or were damaged. In addition, the cells showed fibrous protein deposits that closely resemble Lewy bodies, deposits found in brain cells of Parkinson's patients.

"Together, it's what you see in Parkinson's," Greenamyre said. How rotenone might have triggered these changes in rat is unclear. University of Pennsylvania researchers Benoit I. Giasson and Virginia M.-Y. Lee, who reviewed the Emory experiment, suggest the pesticide might target the mitochondria, a genetic bundle that generates most of a cell's energy.

Such damage unleashes rogue molecules known as free radicals that wreak havoc in cells. Free radicals have been implicated in many degenerative diseases.

"Neurons are particularly sensitive," Giasson and Lee noted. Greenamyre said future rotenone experiments with rats would test new drugs aimed at protecting dopamine-producing cells.

In the meantime, he suggested that farmers and public health agencies reconsider pesticide usage.

"Pesticides are essential for growing crops, but we may need to think about minimizing their environmental impact," he said.

Manganese dioxide exposures and respirator performance at an alkaline battery plant.

Hanley KW, Lenhart SW

National Institute for Occupational Safety and Health, Cincinnati, Ohio, USA.

Two industrial hygiene studies were conducted at an alkaline battery plant to evaluate worker exposures to manganese dioxide particulate and the effectiveness of filtering facepiece respirators. The work areas studied included the plant's powder-processing tower and press rooms where manganese was blended, compacted with graphite, and inserted into battery cans. Full-shift personal breathing zone monitoring was conducted to estimate manganese dust exposures of press operators, mechanics, and material handlers. In-facepiece and personal breathing zone air sampling pairs were also collected using a program protection factor protocol to estimate the protection provided by the respirators. Particle size evaluations were made using nylon cyclones and Marple personal multi-stage impactors. All samples were analyzed for manganese by inductively coupled argon plasma, atomic emission spectroscopy via NIOSH analytical method 7300 utilizing a modified acid digestion procedure. Fifty-four, full-shift, time-weighted average (TWA) exposures to total manganese ranged from 0.1 to 5.4 milligrams per cubic meter (mg/m³); worker exposures were substantially lower during a follow-up study due to engineering control improvements. Concurrent area sample comparisons of total and respirable manganese revealed that the respirable particulate mass fractions ranged from 6 to 32 percent, and mass median aerodynamic diameters determined from personal breathing zone air samples were mostly greater than 10 micrometers. Fifteen respirator performance evaluations were conducted using Moldex 2200 respirators fitted with 25 millimeter cassettes and light weight sampling probes. Protection factors ranged from 5 to 220, with a geometric mean and standard deviation of 31 and 2.97, respectively. The 5th percentile protection factor estimate was 5, as calculated from the protection factor distribution for this sample set. In 1995, the American Conference of Governmental Industrial Hygienists (ACGIH) lowered the elemental and inorganic manganese dust Threshold Limit Value (TLV) from 5 mg/m³ to 0.2 mg/m³ to address adverse pulmonary and central nervous system effects and male infertility. Although most personal breathing zone concentrations were above 0.2 mg/m³, none of the in-facepiece concentrations exceeded this concentration. Parkinson's-like symptoms have been reported in the literature for high manganese dust and fume exposures, but the importance of low dust exposures for producing neurological effects is uncertain.

Nervenarzt 2000 May;71(5):416-9

[Follow-up study after enteral manganese poisoning: clinical, laboratory and neuroradiological findings].

[Article in German]

Degner D, Bleich S, Riegel A, Sprung R, Poser W, Ruther E

Psychiatrische Klinik und Poliklinik, Georg-August-Universitat Gottingen.

Manganese intoxication is an unusual, severe form of intoxication. This report deals with a patient now 80 years old who accidentally ingested a solution of potassium permanganate for a period of at least 4 weeks 14 years ago. Since then, the patient suffers from a mild parkinsonian syndrome and distally accentuated polyneuropathies. Psychiatric disorders, especially demential or depressive symptoms, were not observed. Manganese analysis of his hair still shows a clear increase in manganese concentration. The MRI of his brain showed no pathological changes, in particular none of those often described with symmetric signal elevation in T1 in the area of the basal ganglia. In this study, we present clinical, laboratory, and neuroradiological findings. Unusual in this case with a short exposition is the long duration and clinical improvement without L-dopa treatment.

J Cell Physiol 2000 Oct;185(1):80-6

Role of heme oxygenase-1 in the regulation of manganese superoxide dismutase gene expression in oxidatively-challenged astroglia.

Frankel D, Mehindate K, Schipper HM

Bloomfield Centre for Research in Aging, Lady Davis Institute for Medical Research, Sir Mortimer B. Davis-Jewish General Hospital, Montreal, Canada.

Manganese superoxide dismutase (MnSOD) is an antioxidant enzyme that reduces superoxide anion to hydrogen peroxide in cell mitochondria. MnSOD is overexpressed in normal aging brain and in various central nervous system disorders; however, the mechanisms mediating the upregulation of MnSOD under these conditions remain poorly understood. We previously reported that cysteamine (CSH) and other pro-oxidants rapidly induce the heme oxygenase-1 (HO-1) gene in cultured rat astroglia followed by late upregulation of MnSOD in these cells. In the present study, we demonstrate that antecedent upregulation of HO-1 is necessary and sufficient for subsequent induction of the MnSOD gene in neonatal rat astroglia challenged with CSH or

dopamine, and in astroglial cultures transiently transfected with full-length human HO-1 cDNA. Treatment with potent antioxidants attenuates MnSOD expression in HO-1-transfected astroglia, strongly suggesting that intracellular oxidative stress signals MnSOD gene induction in these cells. Activation of this HO-1-MnSOD axis may play an important role in the pathogenesis of Alzheimer disease, Parkinson disease and other free radical-related neurodegenerative disorders. In these conditions, compensatory upregulation of MnSOD may protect mitochondria from oxidative damage accruing from heme-derived free iron and carbon monoxide liberated by the activity of HO-1. Copyright 2000 Wiley-Liss, Inc.

J Neurosci Res 1999 Apr 15;56(2):113-22

Existing and emerging mechanisms for transport of iron and manganese to the brain.

Malecki EA, Devenyi AG, Beard JL, Connor JR

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The metals iron (Fe) and manganese (Mn) are essential for normal functioning of the brain. This review focuses on recent developments in the literature pertaining to Fe and Mn transport. These metals are treated together because they appear to share several transport mechanisms. In addition, several neurological diseases such as Alzheimer's Disease, Parkinson's Disease, and Huntington's Disease are all associated with Fe mismanagement in the brain, particularly in the striatum and basal ganglia. Similarly, Mn accumulation in brain also appears to target the same brain regions. Therefore, stringent regulation of the concentration of these metals in the brain is essential. The homeostatic mechanisms for these metals must be understood in order to design neurotoxicity prevention strategies.

Arch Neurol 2000 Apr;57(4):597-9

Manganese intoxication.

Lee JW

Department of Neurology, College of Medicine, The Catholic University of Korea, Seoul.

Manganese plays an important role as a cofactor in many enzymatic reactions in humans but in excess amounts can cause irreversible nervous system damage. Although manganism is a rare condition, it can be the cause of complex nervous system symptoms, especially in the setting of environmental exposure. Specifically, manganese is a well-known cause of dystonic parkinsonism. This article highlights several historical descriptions of the clinical manifestations, pathological changes, and attempted therapeutic intervention in manganese intoxication.

Rinsho Shinkeigaku 1999 Jul;39(7):693-9

[Diagnostic utility of positron emission tomography for parkinsonism after chronic manganese exposure].

[Article in Japanese]

Abe Y, Kachi T, Kato T, Ito K, Yanagisawa N, Sobue G

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Positron emission tomography (PET) with [18F] 6-fluoro-L-dopa (18F-FDOPA) was performed in three South Korean patients with parkinsonism who developed after chronic manganese exposure. A 51-year-old man (patient 1) suffered from masked face, marked postural tremor of hands, dystonia in the neck and the upper extremities, severe retropulsion and lateropulsion which were typical for chronic manganese intoxication. 18F-FDOPA scan was normal. Other two patients, a 46-year-old man (patient 2) and a 47-year-old man (patient 3), showed tremor at rest and rigidity predominantly on the right side, bradykinesia, stooped posture and postural instability; all of these were typical for Parkinson's disease (PD). There was reduced uptake of 18F-FDOPA in the striatum, particularly in the posterior putamen predominant on the left side, in both patient 2 and 3. From these results, patient 1 was diagnosed as pure manganism, while patient 2 and 3 were primarily as PD, because loss of nigrostriatal fibers was obvious with asymmetry of affection in the putamen. PET with 18F-FDOPA provides valuable information for differentiation between PD and manganism, although it is not clear whether development of parkinsonian symptoms in patient 2 and 3 was modified by excessive manganese exposure.

J Am Coll Nutr 1999 Oct;18(5):413-23

Multiple antioxidants in the prevention and treatment of Parkinson's disease.

Prasad KN, Cole WC, Kumar B

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Parkinson's disease (PD) is one of the major progressive neurological disorders for which no preventative or long-term effective treatment strategies are available. Epidemiologic studies have failed to identify specific environmental, dietary or lifestyle risk factors for PD except for toxic exposure to manganese, meperidine (Demerol, the "designer drug" version of which often contains a toxic byproduct of the synthesis, 1-methyl-4-phenyl 1,2,3,6 tetrahydropyridine [MPTP]), and some herbicides and pesticides. The search for genetic risk factors such as mutation, overexpression or underexpression of nuclear genes in DA neurons in idiopathic PD has not been successful as yet. Polymorphism in certain genes appears to be a risk factor, but there is no direct evidence for the causal relationship between polymorphism and increased risk of PD. In familial PD, mutation in the alpha-synuclein gene is associated with the disease, but a direct role of this gene in degeneration of DA neurons remains to be established. Although mutations in the Parkin gene has been associated with autosomal recessive juvenile Parkinson's disease, the role of this gene mutation in causing degeneration of DA neurons has not been defined. We have reported that in hereditary PD, a mutation in the alpha-synuclein gene may increase the sensitivity of DA neurons to neurotoxins. We hypothesize that, in idiopathic PD, epigenetic (mitochondria, membranes, protein modifications) rather than genetic events are primary targets which, when impaired, initiate degeneration in DA neurons, eventually leading to cell death. Although the nature of neurotoxins that cause degeneration in DA neurons in PD is not well understood, oxidative stress is one of the intermediary risk factors that could initiate and/or promote degeneration of DA neurons. Therefore, supplementation with antioxidants may prevent or reduce the rate of progression of this disease. Supplementation with multiple antioxidants at appropriate doses is essential because various types of free radicals are produced, antioxidants vary in their ability to quench different free radicals and cellular environments vary with respect to their lipid and aqueous phases. L-dihydroxyphenylalanine (L-dopa) is one of the agents used in the treatment of PD. Since L-dopa is known to produce free radicals during its normal metabolism, the combination of L-dopa with high levels of multiple antioxidants may improve the efficacy of L-dopa therapy.

Neurotoxicology 1999 Apr-Jun;20(2-3):499-507

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A brief history of the neurobehavioral toxicity of manganese: some unanswered questions.

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It was observed by Couper in 1837 that manganese dust produces a neurological syndrome characterized by muscle weakness, tremor, bent posture, whispered speech and excess salivation. The similarity of these symptoms to those of Parkinson's disease were not recognized for many years. In addition to its Parkinson-like effects, manganese produces behavioral symptoms in humans including nervousness, hallucinations, memory loss, cognitive problems, bizarre behaviors and flight of ideas. Despite these signs and symptoms, there have been few systematic attempts to study the effects of manganese on behavior using animal models. The need to better understand the effects of manganese on behavior is becoming more important due to the potential of increased environmental exposure to manganese due to its use, or proposed use as a gasoline additive in a number of countries. However, there is debate as to which manganese compounds should receive priority for testing, what route of administration should be used in this testing, what dosing regimens should be used, what species are appropriate for behavioral testing, and what behavioral tests should be selected. Research to answer these questions is needed so that the behavioral effects of manganese can be described comprehensively and the mechanisms underlying these effects can be understood.

Kao Hsiung I Hsueh Ko Hsueh Tsa Chih 1999 May;15(5):297-301

Rapid progression of parkinsonism associated with an increase of blood manganese.

Kao HJ, Chen WH, Liu JS

Department of Neurology, Kaohsiung Medical College Hospital, Taiwan, Republic of China.

In this paper, we report a 72-year-old man whose parkinsonian pictures accelerated rapidly after an ingestion of unknown herb pills. His serum manganese and aluminum level increased 2-fold and 5-fold over physiological level respectively. A reverse of his parkinsonian deterioration was accompanied with a normalization of these metals. Exclusive heavy metals have been widely mentioned in parkinsonism. While industrial source of these metals has extensively been sought, pharmacology is rarely mentioned in this aspect, especially of herb medicine origin. We suggest that an acceleration of parkinsonian pictures should raise the need to re-evaluate the possibility of heavy metal intoxication in parkinsonism. Besides of industrial

contamination, we should be alert for the nonindustrial source in our population.

Brain Res Mol Brain Res 1999 May 7;68(1-2):22-8

Manganese potentiates nitric oxide production by microglia.

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Manganese toxicity has been associated with clinical symptoms of neurotoxicity which are similar to the symptoms observed in Parkinson's disease. Earlier reports indicated that reactive microglia was present in the substantia nigra of patients with Parkinson's disease. Using N9 microglial cells, the current study was designed to determine whether high levels of manganese were associated with microglial activation. Results indicated that manganese significantly increased the bacterial lipopolysaccharide-induced nitric oxide production. This potent activity of manganese was not shared by other transition metals tested, including iron, cobalt, nickel, copper and zinc. Immunohistochemical staining and Western blot analysis indicated that manganese increased the cellular production of inducible nitric oxide synthase. Northern blot analysis indicated that manganese likely increased iNOS gene transcription since this agent increased the mRNA level of the inducible nitric oxide synthase. In contrast to other transition metals tested, manganese did not appear to be cytotoxic to microglial cells. These results suggested that manganese could induce sustained production of neurotoxic nitric oxide by activated microglial cells, which might cause detrimental consequences to surrounding neurons.

Neurotoxicology 1995 Fall;16(3):511-7

Effects of calcium-deficient diets on manganese deposition in the central nervous system and bones of rats.

Yasui M, Ota K, Garruto RM

Division of Neurological Diseases, Wakayama Medical College, Japan.

The presence of both aluminum (Al) and manganese (Mn) in central nervous system tissues (CNS) has been reported in Parkinson's disease and in parkinsonism-dementia (PD) on Guam. Epidemiological surveys on Guam have suggested that low calcium (Ca), magnesium (Mg) and high Al and Mn in river, soil and drinking water may be implicated in the pathogenesis of PD. Experimentally, low Ca-Mg diets with or without added Al have been found to accelerate Al deposition in the CNS of rats and monkeys. Although excessive deposition of Mn produces similar neurotoxic action to Al in CNS tissues, the mechanism of Mn deposition coupled with Al loading in the presence of low Ca-Mg intake is not yet known. In this study, the deposition and metal-metal interaction of both Al and Mn in the CNS, visceral organs and bones of rats fed unbalanced mineral diets were analyzed. Male Wistar rats, weighing 200 g, were maintained for 90 days on the following diets: (A) standard diet, (B) low Ca diet, (C) low Ca-Mg diet, (D) low Ca-Mg diet with high Al. Al and Mn content were determined in the frontal cortex, spinal cord, kidney, muscle, abdominal aorta, femur and lumbar spine using neutron activation analysis (NAA). Our results demonstrate that serum Ca levels were decreased in the following dietary order: C<D<B<A. Serum Mg levels were significantly lower in rats from Groups C and D, compared with those in Groups A and B, reflecting the content of Mg and other interacting minerals in the diet. There was no significant difference in serum Al, zinc and phosphorus levels. Ca and Mg contents in lumbar vertebrae and the femur were significantly lower and Al levels significantly higher in rats maintained on the low Ca-Mg diet with or without added Al. Al content in CNS tissues and visceral organs were highest in rats fed diets deficient in Ca alone or low in Ca-Mg with or without added Al. Bone Mn levels significantly increased in rats fed the low Ca-Mg diet with added Al. Mn content in the frontal cortex significantly increased in rats fed diets low in Ca-Mg with or without added Al. But the Mn content of other tissues including the spinal cord, kidney, muscle and abdominal aorta was unchanged in rats given Ca deficient diets. Intake of low Ca and Mg with added Al in rats led to the high concentrations of Mn and Al in bones and in the frontal cortex. We conclude that unbalanced mineral diets and metal-metal interactions may lead to the unequal distribution of Al and Mn in bones and ultimately in the CNS inducing CNS degeneration.

J Neurol 1999 Mar;246(3):198-206

Parkinsonism, pyramidal signs, polyneuropathy, and cognitive decline after long-term occupational solvent exposure.

Hageman G, van der Hoek J, van Hout M, van der Laan G, Steur EJ, de Bruin W, Herholz K

Department of Neurology, Medical Spectrum Twente, Hospital Enschede, The Netherlands.

It is well known that exposure to manganese, solvents, or carbon monoxide in an occupational setting may

lead to central nervous system damage and parkinsonism. The most important solvents in this respect are methanol, toluene, carbon disulfide, and n-hexane. We describe three patients who had been exposed to various solvents for more than 20 years (25, 34, and 46 years). They presented with parkinsonism, pyramidal signs, mild cognitive decline, and unresponsiveness to levodopa. Two patients had a predominantly axonal and sensory polyneuropathy of the lower legs with fasciculations in one of them. Parkinsonian features were progressive, even after the patients had stopped work. We present clinical data, neuropsychological findings, and results of brain computed tomography or magnetic resonance imaging, electroneuromyography, evoked potentials, single photon emission computed tomography, and positron-emission tomography. There is growing evidence that various organic solvents give rise to a parkinsonism syndrome with pyramidal features in susceptible individuals.

Mov Disord 2001 May;16(3):565-8

Parkinsonism after glycine-derivate exposure.

Barbosa ER, Leiros Da Costa MD, Bacheschi LA, Scaff M, Leite CC.

Divisao de Clinica Neurologica, do Hospital das Clinicas da Faculdade, de Medicina da Universidade, de Sao Paulo, Sao Paulo, Brazil.

This 54-year-old man accidentally sprayed himself with the chemical agent glyphosate, a herbicide derived from the amino acid glycine. He developed disseminated skin lesions 6 hours after the accident. One month later, he developed a symmetrical parkinsonian syndrome. Two years after the initial exposure to glyphosate, magnetic resonance imaging revealed hyperintense signal in the globus pallidus and substantia nigra, bilaterally, on T2-weighted images. Levodopa/benserazide 500/125 mg daily provided satisfactory clinical outcome.

Scand J Work Environ Health 1994 Aug;20(4):301-5

Parkinsonism after chronic exposure to the fungicide maneb (manganese ethylene-bis-dithiocarbamate).

Meco G, Bonifati V, Vanacore N, Fabrizio E.

Department of Neurosciences, La Sapienza University, Rome, Italy.

Permanent parkinsonism was observed in a man with chronic exposure to the fungicide maneb (manganese ethylene-bis-dithiocarbamate). Symptoms developed at 37 years of age, two years after exposure had ceased. To our knowledge, this is the second report on parkinsonism associated with exposure to maneb. Manganese is a well-known parkinsonigen toxin in humans. More recently, it has been shown that dithiocarbamates can also induce extrapyramidal syndromes. The biochemical effects of manganese and dithiocarbamates are reviewed and their possible neurotoxic mechanisms are discussed. Both of these components may have played a role in this case.

: Neurology 1988 Apr;38(4):550-3

Chronic exposure to the fungicide maneb may produce symptoms and signs of CNS manganese intoxication.

Ferraz HB, Bertolucci PH, Pereira JS, Lima JG, Andrade LA.

Department of Neurology and Neurosurgery, Escola Paulista de Medicina, Sao Paulo, Brazil.

Manganese (Mn) poisoning, a well-known hazard in miners and industrial workers, shares many features with Parkinson's disease. Two young agricultural workers with a parkinsonian syndrome, who mentioned exposure to the fungicide maneb (manganese ethylene-bis-dithiocarbamate), led us to investigate a new possible source of Mn intoxication. Fifty male rural workers with occupational exposure to maneb were compared with 19 rural workers without fungicide exposure. We noted significantly higher prevalence of plastic rigidity with cogwheel phenomenon, headache, fatigue, nervousness, memory complaints, and sleepiness in the exposed group. In addition, we saw other neurologic signs, such as postural tremor, cerebellar signs, and bradykinesia, although without statistical significance. The data suggest that occupational exposure to pesticides containing Mn is a possible source of Mn intoxication of the CNS.

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PHEOCHROMOCYTOMA

Pheochromocytoma is a disease, which seems to bear many similarities to hyperthyroidism, especially in that it seems to involve a copper deficiency. However, the key deficiency in pheochromocytoma appears to be chromium.

Pheochromocytoma (or pheo for short) involves the growth of pheo tumors, which can be located in the adrenals or anywhere in the body and which produce excessive amounts of catecholamine hormones, such as epinephrine (adrenalin) and norepinephrine (noradrenalin).

The effect is that the person with pheo tumors has high levels of these hormones circulating which puts the person in a constant state of extreme stress.

Pheochromocytoma is usually considered a hereditary disease since it runs in families, but random occurrences exist, pointing to other possible causes. One study below is suggestive in indicating that if the father is exposed to urethane or chromium (III) before conception, the offspring may get pheochromocytoma.

Besides the above theory that pheochromocytoma is the result of genetic or other damage to the father from chemical exposure, I'm also looking at the following possible disease etiology:

Some minerals seem to play a role in the generation of pheochromocytoma. Excessive manganese may stimulate the growth of pheo cells and this may be a result of a chromium deficiency in pheos. High manganese foods should probably be limited. These include: bananas, blueberries, pineapples, eggs, whole grains, green vegetables, legumes, nuts, rice, eggs, and ginger.

Also iron seems to be involved. Iron appears to be necessary in the formation of catecholamine hormones. Excessive manganese (or excessive cellular manganese caused by a chromium deficiency) may deplete iron, thus forcing the body to produce tumors as additional manufacturing sites for the production of catecholamine hormones. When iron is replenished, the tumors over-produce and pheo symptoms result.

Copper seems to be essential for forming monoamine oxidase and other enzymes which break down the catecholamines. Since manganese is a copper antagonist, the excessive manganese causes a copper deficiency which in turn causes a depletion of monoamine oxidase and a subsequent excess of catecholamines.

My interpretation of the first study below is this: Pheochromocytoma is a tumor of the chromaffin cells of the adrenal glands. Chromaffin tissue is named this from "chromium" and "affinis", which means having affinity for. The chromaffin tissue takes up and stains strongly with chromium salts. This means that these tissues normally need large amounts of chromium.

In the study below, exposure of male mice to chromium before conception caused an adaptive genetic change in the offspring to prepare them for an environment where chromium levels and intake will be high. This adaptation probably increases the excretion of chromium in the offspring to prevent toxicity. However, if the offspring are then reared in a chromium-normal environment, the chromaffin cells become chromium-deficient and tumors then grow as an adaptation to increase chromium extraction from the blood supply. These tumors are pheochromocytomas and they result not from genetic "damage" but from genetic "adaptation."

Other studies show that manganese, which is a chromium antagonist, increases the growth of pheo tumors, which offers further support to the thesis that pheos result from a chromium deficiency. If this analysis is correct, then pheochromocytoma may be helped significantly by supplementing with high amounts of chromium, perhaps as high as 1000 mcg or more. Please be aware that this is just a theory based upon the present studies.

Toxicol Appl Pharmacol 1999 Jul 15;158(2):161-76

Preconception urethane or chromium(III) treatment of male mice: multiple neoplastic and non-neoplastic changes in offspring.

Yu W, Sipowicz MA, Haines DC, Birely L, Diwan BA, Riggs CW, Kasprzak KS, Anderson LM

Division of Basic Sciences, National Cancer Institute, Frederick, Maryland, 21702, USA.

Increase in neoplasia in offspring after preconception exposure of parents presents puzzling features such as high frequency of effects and lack of Mendelian inheritance. The present study examined the hypothesis that preconception carcinogenesis involves an increase in the rate of occurrence of neoplasms with a spontaneous incidence. Male NIH Swiss mice (12 per group) were exposed 2 weeks before mating (once, ip) to urethane (1.5 g/kg) or chromium(III) chloride (1 mmol/kg). Offspring (48-78/sex/group) were examined for all grossly apparent changes when moribund or at natural death, followed by histopathological diagnosis and statistical analysis. Significant exposure-related changes occurred in multiple organs. Ten to 20 percent of offspring showed changes related to paternal exposure, including at least one sired by most treated males. Pheochromocytomas occurred in both male and female offspring after both treatments, with none in controls. These neoplasms are rare in mice and suggest endocrine dysfunction as a component of preconception carcinogenesis. This was supported by increases in thyroid follicular cell and Harderian gland tumors, ovarian cysts, and uterine abnormalities. Lung tumors were increased in female offspring only. Effects seen in offspring only after paternal urethane exposure were an increase in preneoplasia/neoplasia in the glandular stomach (males) and in females, increased lymphoma but

decreased incidence of histiocytic sarcoma. Increases in incidence of male reproductive gland tumors and of renal non-neoplastic lesions occurred only after chromium exposure. Thus, preconception exposure of fathers to toxicants had a significant impact on both neoplastic and non-neoplastic changes in almost all tissues in which these lesions often occur naturally during the aging process. Copyright 1999 Academic Press.

Title

Serotonin metabolism and platelet monoamine oxidase activity in patients with medullary carcinoma of the thyroid and pheochromocytoma.

Author

Feldman JM; Farrell RE; Wells SA Jr

Source

Am J Med Sci, 278(1):39-48 1979 Jul-Aug

Abstract

Occasional patients with medullary carcinoma of the thyroid (Multiple Endocrine Neoplasia Type II [MEN II]) are reported to have excessive serotonin (5-HT) production from the MCT; almost all patients with metastatic MCT have elevations in plasma concentration of the amine oxidase, histaminase. The elevated 5-HT production is thought to contribute to the troublesome diarrhea experienced by patients with MEN II. We compared the urinary excretion of 5-hydroxyindoleacetic acid (5-HIAA), the principle metabolite of 5-HT, of 33 patients with MCT with the urinary excretion of 5-HIAA in 33 control subjects. Six of the 33 MCT patients (18%) had severe diarrhea. The 5-HIAA excretion of the MCT patients did not differ from that of normal subjects. We also compared the platelet monoamine oxidase (MAO) activity of 27 MCT patients and 27 control subjects. The platelet MAO activity of the two groups did not differ. The 5-HT content and MAO activity of 6 of the MCTs was similar to normal thyroid tissue. The MAO activity of two follicular adenomas of the thyroid was greater than the MAO activity of MCTs. In contrast to the uniform elevation of plasma histaminase in patients with MCT, the platelet MAO activity is not altered and the majority of MCTs do not produce excessive amounts of 5-HT.

My interpretation of the following study is that the high calcium intake of bulls, not counterbalanced by calcium losses which cows have from lactation, causes excess calcitonin production which leads to ultimobranchial neoplasms, multiple endocrine tumors, and pheochromocytoma. Perhaps the solution is to increase magnesium intake and limit calcium intake. Also, a copper deficiency could be involved because copper is essential for magnesium metabolism.

Title

"Aging bull".

Author

Geelhoed GW

Address

George Washington University Medical Center, Washington, DC, USA.

Source

Med Hypotheses, 47(6):471-9 1996 Dec

Abstract

An old bull, it is said by those who know, can have his troubles. Included among these are vertebral osteosclerosis and ankylosing spondylosis; this stiffening up limits, rather than accentuates, the value and reproductive potential of a stud bull past his prime. Associated with these abnormalities, however-and not seen in age-matched cows of comparable breeds-are fascinating endocrine neoplasms suggestive of a pattern that could be productive as a model of human hereditary endocrine abnormalities. Adjacent to the thyroid gland in other vertebrates are ultimobranchial bodies that are incorporated into the lateral thyroid lobes in primates as the parafollicular 'C cells' of the thyroid. These are the cells in man that give rise to medullary thyroid cancer and are associated with calcitonin secretion, useful as a tumor marker. In aging bulls of whatever breed, nearly half exhibit abnormality of these ultimobranchial bodies: 20% show hyperplasia, and 30% have frank neoplasia. These ultimobranchial tumors appear in bulls passing 6 1/2 years in age, and are absent in young bulls and all cows of any age. Calcitonin can be demonstrated in the ultimobranchial tumors from bulls, and secretion is stimulated by *calcium* infusion, though serum *calcium* remains normal. The ultimobranchial tumors themselves can range from hyperplasia through adenoma to metastasizing carcinoma-in fact, representing one of the commoner cattle cancers. Parathyroid glands taken from bulls with these ultimobranchial tumors initially show evidence of inhibited secretory activity and morphologic atrophy, but later go on to develop hyperplasia and, eventually, autonomy. Cattle forage on *calcium*-rich diets. Bulls appear to respond to this *calcium* excess from the positive balance, but breeding cows have the unique *calcium* deficits of the high net loss of *calcium* through lactation and the large requirements of calcifying a fetal skeleton. Chronic stimulation of the APUD-derived ultimobranchial bodies by high *calcium* intake, not counterbalanced by calcium losses in the bulls, may account for the development over time of the ultimobranchial neoplasms. Further, a number of the bulls who have the ultimobranchial tumors are found to have multiple endocrine tumors in other glands-bilateral pheochromocytomas and pituitary acidophil adenomas.

Klin Wochenschr 1981 Oct 15;59(20):1165-73

[The influence of different diets and smoking on the clinical chemical diagnosis of pheochromocytoma, neuroblastoma, and carcinoid syndrome].

[Article in German]

Heinemann G, Schievelbein H, Eberhagen D, Rahlfs V

The interference of various foodstuffs on methods to determine epinephrine (E), norepinephrine (NE), vanillylmandelic acid (VMA), metanephrines (MN), homovanillic acid (HVA), and 6-hydroxyindole acetic acid (5-HIA) in the 24 h urine for diagnosis of pheochromocytoma and carcinoid syndrome, respectively, was investigated. The foodstuffs included were: tea, coffee, almonds, pineapples, cheese, walnuts, vanilla pudding, bananas, tomatoes, and chocolate. Further, the interference of cigarette smoking on the determination of E, NE, VMA, and MN was also investigated. Walnuts caused a rather high elevation of 5-HIA in the urine. After eating bananas elevated excretion of E, NE, VMA, MN, and 5-HIA was observed. Small increases of the MN values were noticed after coffee and pineapples. Smoking of 20-30 cigarettes/day had no influence on the variables measured. If the methods described are used, thus, only bananas and walnuts have to be restricted some days before and during urine sampling, but not coffee and pineapples if consumed in the usual small quantities. There is no reason to insist on diet restriction except for bananas and walnuts.

PMID: 7300237, UI: 82056396

The following study shows that manganese stimulates the growth of pheochromocytoma cells.

Activation of ERK1 and ERK2 is required for manganese-induced neurite outgrowth in rat pheochromocytoma (PC12) cells.

Walowitz JL, Roth JA

Department of Pharmacology and Toxicology, State University of New York at Buffalo, School of Medicine and Biomedical Sciences, Buffalo 14214, USA.

Mn(2+) treatment has been shown to promote neurite outgrowth in rat pheochromocytoma (PC12) cells in a time- and dose-dependent manner. This process is mediated through the interactions of extracellular matrix (ECM) proteins and integrin receptors. Studies were performed to determine whether the phosphorylation of the MAP kinases, ERK1 and 2, is required for Mn(2+)-induced neurite outgrowth. A time- and dose-dependent increase in phosphorylation of both ERK1 and 2 was observed upon treatment of PC12 cells with Mn(2+). Phosphorylation of the ERKs occurred as early as 2 hr after initiating treatment, with a maximum increase occurring at approximately 24 hr. Inhibition of MEK with the specific inhibitor, PD98059, blocked the phosphorylation of ERK1 and 2 and increased Mn(2+) toxicity. When cells were grown in serum-free defined medium, Mn(2+)-induced phosphorylation of ERK1 and ERK2 occurred in cells grown on surfaces treated with growth serum or fibronectin but not on surfaces treated with poly-L-lysine. In addition, the pentapeptide GRGDS, which blocks RGD-mediated interactions, inhibited Mn(2+)-induced phosphorylation of ERK1 and 2. The Mn(2+)-induced increase in phosphorylated ERK1 and 2 was not seen in a PC12 cell line that does not respond to Mn(2+). These data support the hypothesis that integrin-mediated activation of the MAPK signal transduction pathway leading to the activation of ERK1 and 2 is required for Mn(2+)-induced PC12 differentiation and neurite outgrowth. Copyright 1999 Wiley-Liss, Inc.

PMID: 10467256, UI: 99398497

J Neurosci 1998 Jan 15;18(2):687-97

Mitochondrial manganese superoxide dismutase prevents neural apoptosis and reduces ischemic brain injury: suppression of peroxynitrite production, lipid peroxidation, and mitochondrial dysfunction.

Keller JN, Kindy MS, Holtsberg FW, St Clair DK, Yen HC, Germeyer A, Steiner SM, Bruce-Keller AJ, Hutchins JB, Mattson MP

Molecular and Cell Biology Division, Department of Biological Sciences, University of Kentucky, Lexington, Kentucky 40536, USA.

Oxidative stress is implicated in neuronal apoptosis that occurs in physiological settings and in neurodegenerative disorders. Superoxide anion radical, produced during mitochondrial respiration, is involved in the generation of several potentially damaging reactive oxygen species including peroxynitrite. To examine directly the role of superoxide and peroxynitrite in neuronal apoptosis, we generated neural cell lines and transgenic mice that overexpress human mitochondrial manganese superoxide dismutase (MnSOD). **In cultured pheochromocytoma PC6 cells, overexpression of mitochondria-localized MnSOD prevented apoptosis induced by Fe2+, amyloid beta-peptide (Abeta), and nitric oxide-generating agents.** Accumulations of peroxynitrite, nitrated proteins, and the membrane lipid peroxidation product 4-hydroxynonenal (HNE) after exposure to the apoptotic insults were markedly attenuated in cells expressing MnSOD. **Glutathione peroxidase activity levels were increased in cells overexpressing MnSOD, suggesting a compensatory response to increased H2O2 levels.** The peroxynitrite scavenger uric acid and the antioxidants propyl gallate and glutathione prevented apoptosis induced by each apoptotic insult, suggesting central roles for peroxynitrite and membrane lipid peroxidation in oxidative stress-induced apoptosis. Apoptotic insults decreased mitochondrial transmembrane potential and energy charge in control cells but not in cells overexpressing MnSOD, and cyclosporin A and caspase inhibitors protected cells against apoptosis, demonstrating roles for mitochondrial alterations and caspase activation in the apoptotic process. Membrane lipid peroxidation, protein nitration, and neuronal death after focal cerebral ischemia were significantly reduced in transgenic mice overexpressing human MnSOD. The data suggest that mitochondrial superoxide accumulation and consequent peroxynitrite production and mitochondrial dysfunction play pivotal roles in neuronal apoptosis induced by diverse insults in cell culture and in vivo.

PMID: 9425011, UI: 98086321

J Urol 1995 Jun;153(6):1787-90

Remarkably suppressed manganese superoxide dismutase activity in malignant pheochromocytoma.

Nakada T, Kubota Y, Sasagawa I, Yagisawa T, Watanabe M, Ishigooka M

Department of Urology, Yamagata University, School of Medicine, Japan.

There are almost no special histopathological characteristics or criteria that exactly define a malignant pheochromocytoma. Tissue concentrations of catecholamine metabolites and superoxide dismutase activity have been proposed as possible candidates for discriminating between benign and malignant pheochromocytomas. Tissue concentrations of dihydroxyphenylalanine, metanephrine, normetanephrine, vanillylmandelic acid, and 3-methoxy-4-hydroxyphenylethylglycol were determined in 29 normal adrenal medullas, 13 benign pheochromocytomas and 6 malignant pheochromocytomas, respectively. The copper-zinc superoxide dismutase and manganese superoxide dismutase activities in remnants of these tissues were determined by interruption of nitric formation from hydroxylamines. Catecholamine metabolites and copper-zinc superoxide dismutase activity in benign and malignant pheochromocytomas were identical. Manganese superoxide dismutase activity in malignant pheochromocytoma was the lowest among the groups examined. These data suggest that the assay of catecholamine metabolites in removed specimens is not a reliable method for making a differential diagnosis of benign or malignant pheochromocytoma. However, a low level of manganese superoxide dismutase activity in malignant pheochromocytoma may be a marker for malignancy of this neoplasm.

PMID: 7752317, UI: 95271750

J Neurosci Res 1993 Apr 1;34(5):546-61

Manganese induces spreading and process outgrowth in rat pheochromocytoma (PC12) cells.

Lin WH, Higgins D, Pacheco M, Aletta J, Perini S, Marcucci KA, Roth JA

Department of Pharmacology and Therapeutics, School of Medicine and Biomedical Science, State University of New York, Buffalo.

Mn2+ has been shown to promote cell-substrate adhesion and cell spreading in many cell culture systems. **In this study, we present data demonstrating that Mn2+ not only promotes spreading, but also induces process outgrowth in rat pheochromocytoma (PC12) cells. In the presence of 1.0 mM MnCl2, cell spreading was apparent by 6 hr, and nearly 50% of the exposed cells extended neurite-like processes.** These morphological effects of Mn2+ were both time- and dose-dependent. In the presence of cycloheximide, a protein synthesis

inhibitor, both Mn(2+)-induced spreading and neurite outgrowth were prevented, indicating that de novo protein synthesis is required for the effects of Mn2+ to take place. Of the other divalent cations tested, Mg2+, Cd2+, Cu2+, Ni2+, and Zn2+ were ineffective, and only Co2+ partially mimicked the effects of Mn2+. Although Mn(2+)-induced cell adhesion and spreading have been extensively studied, this is the first report that this divalent cation can cause neurite outgrowth. The neurite outgrowth-promoting effects of Mn2+ were distinct from those of nerve growth factor in that the response to Mn2+ was considerably more rapid, but apparently lacked the ability to sustain continuous outgrowth and networking of neurites. Mn2+ also induced the levels of GAP-43 and peripherin, two proteins associated with neuronal differentiation of PC-12 cells. In cells grown in serum-free defined medium, Mn2+ was capable of promoting neurite outgrowth when the cells were plated on surfaces pretreated with normal growth medium, vitronectin, or fibronectin, while it failed to cause these morphological changes in cells plated on untreated or poly-D-lysine-coated substrata. Similarly, Mn2+ also promoted neurite outgrowth from rat sympathetic neurons attached to laminin-treated substrate, but had no effect on neurons maintained on substrate with polylysine only. The pentapeptide Gly-Arg-Gly-Asp-Ser nearly completely prevented the morphological effects of Mn2+ on PC12 cells. These findings are consistent with a hypothesis that Mn(2+)-mediated alteration of an RGD-dependent extracellular matrix-integrin interaction is responsible for the neurotogenic effects.

Toxicology 1991 Apr 8;67(2):129-42

Dopamine metabolism alterations in a manganese-treated pheochromocytoma cell line (PC12).

Vescovi A, Facheris L, Zaffaroni A, Malanca G, Parati EA

Laboratory of Cellular Neuropharmacology, National Neurological Institute C. Besta, Milan, Italy.

By monitoring dopamine metabolism in rat pheochromocytoma derived PC12 cell cultures during extended treatment with manganese chloride, we assessed the functional changes occurring in a dopaminergic system during the development of manganese-induced damage. Besides eliciting a specific toxic effect on PC12 cells, manganese induced the complete disappearance of extracellular (free) but not intracellular (vesicle stored) dopamine and its metabolite 3,4-dihydroxyphenylacetic acid. This effect was observed also using low manganese concentrations (1 microM) and mainly occurred by non-enzymatic catechol oxidation since it was still evident in a cell free medium and it was fully prevented by ascorbic acid but not by reduced glutathione. The possibility of a mere "non-biological" action was ruled out by the observation of an irreversible effect of manganese as manifested by the cells' apparent inability to release dopamine or 3,4-dihydroxyphenylacetic acid into the culture medium even after complete manganese removal (post-manganese incubation). That a free radical mechanism was not involved in the genesis of this irreversible effect was shown by the fact that neither ascorbic acid, catalase, superoxide dismutase nor glutathione-peroxidase were able to prevent the decrease in catecholamine levels in the "post-manganese" incubation medium when added at the same time as the manganese. The results establish this PC12 cell system as an in vitro model for studying interactions between manganese and catechols and provide a detailed description of the nature of the neurochemical alterations that this heavy metal can induce in a dopaminergic system.

PMID: 2031248, UI: 91233477

J Urol 1987 Jul;138(1):9-13

Low level of superoxide dismutase activity in pheochromocytoma.

Nakada T, Koike H, Katayama T

A copper-zinc superoxide dismutase found in the cytosol and intermembrane space of mitochondria, and a manganese superoxide dismutase detected in the mitochondria were determined in pheochromocytomas and normal adrenal tissues. Manganese superoxide dismutase activity in pheochromocytomas was lower than that in the normal adrenal tissues but copper-zinc superoxide dismutase activity was almost identical. The total catecholamine content in pheochromocytomas was greater than that in the normal adrenal tissues, and negative relationships were noted between superoxide dismutase activities and total catecholamine content in pheochromocytomas alone. The low level of manganese superoxide dismutase activity might be a characteristic of pheochromocytomas and the decrease in manganese superoxide dismutase activity may not be attributed solely to a decrease in the amount of mitochondria but to a nonspecific abnormality in mitochondrial enzymes.

Pharmacol Toxicol 1997 Feb;80(2):76-84

Dopamine and iron induce apoptosis in PC12 cells.

Velez-Pardo C, Jimenez Del Rio M, Verschuere H, Ebinger G, Vauquelin G

Department of Protein Chemistry, Free University Brussels (VUB), Belgium.

Recent studies have shown that Fe2+ increases the oxidation of monoamines such as serotonin, dopamine and related toxins and that the formed oxidation products can undergo co-valent binding to free sulphhydryl groups of proteins such as actin and "serotonin binding proteins" which are present in soluble brain extracts. Here we have tested the ability of ferrous iron to induce [3H]dopamine association to cytoplasmic proteins and we have established that a similar oxidation mechanism evidenced in vitro studies could be applied in cell culture. When PC12 cells were incubated with ferrous iron (ferrocene), the binding of [3H]dopamine to proteins was found to be two fold increased with respect to control. The iron is likely to accelerate the oxidation of dopamine to produce quinones which covalently bind to proteins and induce high-molecular protein aggregates. We evidenced that dopamine/iron combination induced cell death in undifferentiated PC12 cells via an active cellular process evaluated in terms of morphological and biochemical changes indicative of apoptosis. We also demonstrated induction of lipid peroxidation when dopamine and ferrocene were present in high concentrations. Moreover, ascorbic acid diminished apoptosis but not the lipid peroxidation process. It might indicate that ferrocene and dopamine could produce oxidative stress of a different nature. These results show that the actions of dopamine and iron are essential in the induction of apoptosis and lipid peroxidation. However, there is no necessary casual link between lipid peroxidation and apoptosis. Our data also suggest that iron is capable of increasing the cytotoxicity of dopamine merely by increasing its rate of oxidation and without intervention of the monoamine oxidase B enzyme and, hence, both phenomena may occur independently from each other in rat pheochromocytoma PC12. These observations may have relevance to the understanding of the mechanism by which dopaminergic neurones are destroyed in some neurodegenerative disorders.

PMID: 9060038, UI: 97213273

Title

Serotonin metabolism and platelet monoamine oxidase activity in patients with medullary carcinoma of the thyroid and pheochromocytoma.

Author

Feldman JM; Farrell RE; Wells SA Jr

Source

Am J Med Sci, 278(1):39-48 1979 Jul-Aug

Abstract

Occasional patients with medullary carcinoma of the thyroid (Multiple Endocrine Neoplasia Type II [MEN II]) are reported to have excessive

serotonin (5-HT) production from the MCT; almost all patients with metastatic MCT have elevations in plasma concentration of the amine oxidase, histaminase. The elevated 5-HT production is thought to contribute to the troublesome diarrhea experienced by patients with MEN II. We compared the urinary excretion of 5-hydroxyindoleacetic acid (5-HIAA), the principle metabolite of 5-HT, of 33 patients with MCT with the urinary excretion of 5-HIAA in 33 control subjects. Six of the 33 MCT patients (18%) had severe diarrhea. The 5-HIAA excretion of the MCT patients did not differ from that of normal subjects. We also compared the platelet monoamine oxidase (MAO) activity of 27 MCT patients and 27 control subjects. The platelet MAO activity of the two groups did not differ. The 5-HT content and MAO activity of 6 of the MCTs was similar to normal thyroid tissue. The MAO activity of two follicular adenomas of the thyroid was greater than the MAO activity of MCTs. In contrast to the uniform elevation of plasma histaminase in patients with MCT, the platelet MAO activity is not altered and the majority of MCTs do not produce excessive amounts of 5-HT.

The following study suggests that pheochromocytoma PC6 cells over express manganese superoxide dismutase (MnSOD). This is perhaps another reason that manganese should be restricted in pheochromocytoma.

J Neurosci 1998 Jan 15;18(2):687-97

Mitochondrial manganese superoxide dismutase prevents neural apoptosis and reduces ischemic brain injury: suppression of peroxynitrite production, lipid peroxidation, and mitochondrial dysfunction.

Keller JN, Kindy MS, Holtzberg FW, St Clair DK, Yen HC, Germeyer A, Steiner SM, Bruce-Keller AJ, Hutchins JB, Mattson MP

Molecular and Cell Biology Division, Department of Biological Sciences, University of Kentucky, Lexington, Kentucky 40536, USA.

Oxidative stress is implicated in neuronal apoptosis that occurs in physiological settings and in neurodegenerative disorders. Superoxide anion radical, produced during mitochondrial respiration, is involved in the generation of several potentially damaging reactive oxygen species including peroxynitrite. To examine directly the role of superoxide and peroxynitrite in neuronal apoptosis, we generated neural cell lines and transgenic mice that overexpress human mitochondrial manganese superoxide dismutase (MnSOD). **In cultured pheochromocytoma PC6 cells, overexpression of mitochondria-localized MnSOD prevented apoptosis induced by Fe2+, amyloid beta-peptide (Abeta), and nitric oxide-generating agents.** Accumulations of peroxynitrite, nitrated proteins, and the membrane lipid peroxidation product 4-hydroxynonenal (HNE) after exposure to the apoptotic insults were markedly attenuated in cells expressing MnSOD. Glutathione peroxidase activity levels were increased in cells overexpressing MnSOD, suggesting a compensatory response to increased H2O2 levels. The peroxynitrite scavenger uric acid and the antioxidants propyl gallate and glutathione prevented apoptosis induced by each apoptotic insult, suggesting central roles for peroxynitrite and membrane lipid peroxidation in oxidative stress-induced apoptosis. Apoptotic insults decreased mitochondrial transmembrane potential and energy charge in control cells but not in cells overexpressing MnSOD, and cyclosporin A and caspase inhibitors protected cells against apoptosis, demonstrating roles for mitochondrial alterations and caspase activation in the apoptotic process. Membrane lipid peroxidation, protein nitration, and neuronal death after focal cerebral ischemia were significantly reduced in transgenic mice overexpressing human MnSOD. The data suggest that mitochondrial superoxide accumulation and consequent peroxynitrite production and mitochondrial dysfunction play pivotal roles in neuronal apoptosis induced by diverse insults in cell culture and in vivo.

The following study shows that manganese exposure on a low protein diet will result in a significant increase in dopamine and norepinephrine levels. Norepinephrine is one of the catecholamine stress hormones and high levels can induce hypertension. I wish that the authors had looked at chromium levels. A low protein diet usually means a high carbohydrate diet which will deplete chromium. Since chromium is an antagonist of manganese, it is possible that the effect is not due per se to low protein but to a combination of high manganese with low chromium. This may offer support to the hypothesis that high manganese and low chromium are involved in pheochromocytoma.

Neurobehav Toxicol Teratol 1985 Sep-Oct;7(5):427-31

Effect of low protein diet on manganese neurotoxicity: III. Brain neurotransmitter levels.

Ali MM, Murthy RC, Mandal SK, Chandra SV

The effect of concurrent low protein (10% casein) diet and manganese (Mn) exposure (3 mg/ml drinking water) on brain levels of dopamine (DA), norepinephrine (NE) and 5-hydroxytryptamine (5-HT) were investigated in Fo-growing (90 days exposure), Fo-diet rehabilitated (low----normal protein diet-28 days) and F1-weaned rats. Mn exposure in either diet group resulted in a significant increase in the DA and NE levels but a decrease in the 5-HT level. These effects were more pronounced in the rats fed the low protein diet, especially in the F1-offsprings. Diet rehabilitation reduced the effects of Mn exposure.

Toxicology 1997 Feb 14;117(1):45-53

Biphasic effects of chromium compounds on catecholamine secretion from bovine adrenal medullary cells.

Liu PS, Lin MK

Department of Microbiology, Soochow University, Taipei, Taiwan, Peoples Republic of China.

CrO3 was found to affect norepinephrine release in a biphasic manner: at concentrations above 100 microM, it inhibited, while at concentrations below 10 microM, it enhanced DMPP- and high K+-induced [3H]norepinephrine (NE) release from bovine adrenal medullary cells. Similar effects were found for K2Cr2O7. CrO3 inhibited the 45Ca2+ uptake induced by DMPP and high K+, suggesting that the voltage-gated Ca2+ channels are possible sites of the inhibitory action of CrO3. CrCl3, possessing a trivalent state in contrast to the hexavalent states of CrO3, K2Cr2O7, inhibited DMPP-induced [3H] release and inhibited, to a lesser extent, high K+-induced [3H]-NE release, suggesting that nicotinic receptors are also possible sites of Cr3+ action. In medullary cells permeabilized with digitonin, both CrO3 and CrCl3 induced [3H]-NE release from cells preloaded with [3H]-NE. In intact cells, CrO3 but not CrCl3 enhanced secretagogue-induced [3H]-NE release and entered into the cells as demonstrated by fluorescence quenching experiments. These results suggest that chromium compounds can induce catecholamine secretion after entering the cytoplasm. The enhancement of norepinephrine release induced by chromium ions appears to be due to interference with the intracellular functions of Ca2+ in the cytoplasm.

Biphasic effects of chromium compounds on catecholamine secretion from bovine adrenal medullary cells.

Liu PS, Lin MK

Department of Microbiology, Soochow University, Taipei, Taiwan, Peoples Republic of China.

CrO₃ was found to affect norepinephrine release in a biphasic manner: at concentrations above 100 microM, it inhibited, while at concentrations below 10 microM, it enhanced DMPP- and high K⁺-induced [3H]norepinephrine (NE) release from bovine adrenal medullary cells. Similar effects were found for K₂Cr₂O₇. CrO₃ inhibited the 45Ca²⁺ uptake induced by DMPP and high K⁺, suggesting that the voltage-gated Ca²⁺ channels are possible sites of the inhibitory action of CrO₃. CrCl₃, possessing a trivalent state in contrast to the hexavalent states of CrO₃, K₂Cr₂O₇, inhibited DMPP-induced [3H] release and inhibited, to a lesser extent, high K⁺-induced [3H]-NE release, suggesting that nicotinic receptors are also possible sites of Cr³⁺ action. In medullary cells permeabilized with digitonin, both CrO₃ and CrCl₃ induced [3H]-NE release from cells preloaded with [3H]-NE. In intact cells, CrO₃ but not CrCl₃ enhanced secretagogue-induced [3H]-NE release and entered into the cells as demonstrated by fluorescence quenching experiments. These results suggest that chromium compounds can induce catecholamine secretion after entering the cytoplasm. The enhancement of norepinephrine release induced by chromium ions appears to be due to interference with the intracellular functions of Ca²⁺ in the cytoplasm.

Natl Toxicol Program Tech Rep Ser 2001 Jul;499:1-343

Toxicology and carcinogenesis studies of indium phosphide (cas no. 22398-90-7) in f344/N rats and b6c3f1 mice (inhalation studies).

National Toxicology Program.

Indium phosphide is used to make semiconductors, injection lasers, solar cells, photodiodes, and light-emitting diodes. Indium phosphide was nominated for study because of its widespread use in the microelectronics industry, the potential for worker exposure, and the absence of chronic toxicity data. Male and female F344/N rats and B6C3F1 mice were exposed to indium phosphide (greater than 99% pure) by inhalation for 14 weeks or 2 years. The frequency of micronuclei was determined in the peripheral blood of mice exposed to indium phosphide for 14 weeks. 14-WEEK STUDY IN RATS: Groups of 10 male and 10 female rats were exposed to particulate aerosols of indium phosphide with a mass median aerodynamic diameter of approximately 1.2 μ m at concentrations of 0, 1, 3, 10, 30, or 100 mg/m³ by inhalation, 6 hours per day, 5 days per week (weeks 1 through 4 and weeks 10 through 14) or 7 days per week (weeks 5 through 9) to accommodate a concurrent teratology study. One male in the 100 mg/m³ group died before the end of the study. Body weight gains of all males and females exposed to 100 mg/m³ were less than those of the chamber controls. As a result of indium phosphide exposure, the lungs of all exposed rats had a gray to black discoloration and were significantly enlarged, weighing 2.7- to 4.4-fold more than those of the chamber controls. Indium phosphide particles were observed throughout the respiratory tract and in the lung-associated lymph nodes. A spectrum of inflammatory and proliferative lesions generally occurred in the lungs of all exposed groups of rats and consisted of alveolar proteinosis, chronic inflammation, interstitial fibrosis, and alveolar epithelial hyperplasia. Pulmonary inflammation was attended by increased leukocyte and neutrophil counts in the blood. The alveolar proteinosis was the principal apparent reason for the increase in lung weights. Indium phosphide caused inflammation at the base of the epiglottis of the larynx and hyperplasia of the bronchial and mediastinal lymph nodes. Exposure to indium phosphide affected the circulating erythroid mass. It induced a microcytic erythrocytosis consistent with bone marrow hyperplasia and hematopoietic cell proliferation of the spleen. Hepatocellular necrosis was suggested by increased serum activities of alanine aminotransferase and sorbitol dehydrogenase in all exposed groups of males and in 10 mg/m³ or greater females and was confirmed microscopically in 100 mg/m³ males and females. 14-WEEK STUDY IN MICE: Groups of 10 male and 10 female mice were exposed to particulate aerosols of indium phosphide with a mass median aerodynamic diameter of approximately 1.2 μ m at concentrations of 0, 1, 3, 10, 30, or 100 mg/m³ by inhalation, 6 hours per day, 5 days per week (weeks 1 through 4 and weeks 10 through 14) or 7 days per week (weeks 5 through 9). Although the effects of indium phosphide exposure were similar in rats and mice, mice were more severely affected in that all males and females in the 100 mg/m³ groups either died or were removed moribund during the study. One male and three females in the 30 mg/m³ group were also removed before the end of the study. In general, body weight gains were significantly less in males and females exposed to 3 mg/m³ or greater compared to those of the chamber controls. Mice exposed to 30 or 100 mg/m³ were lethargic and experienced rapid, shallow breathing. As in rats, lungs were discolored and enlarged 2.6- to 4.1-fold greater than those of chamber controls due to the exposure-induced alveolar proteinosis. Indium phosphide particles were observed in the nose, trachea, larynx, and lymph nodes of some exposed males and females. Alveolar proteinosis, chronic active inflammation, interstitial fibrosis, and alveolar epithelial hyperplasia were observed; these effects were more severe than in rats. Hyperplasia in the bronchial lymph nodes and squamous metaplasia, necrosis, and suppurative inflammation of the larynx were observed in some exposed males and females. Exposure to indium phosphide induced a microcytic erythrocytosis which was consistent with the observed hematopoietic cell proliferation of the spleen. 2-YEAR STUDY IN RATS: Groups of 60 male and 60 female rats were exposed to particulate aerosols of indium phosphide at concentrations of 0, 0.03, 0.1, or 0.3 mg/m³, 6 hours per day, 5 days per week, for 22 weeks (0.1 and 0.3 mg/m³ groups) or 105 weeks (0 and 0.03 mg/m³ groups). Animals in the 0.1 and 0.3 mg/m³ group were maintained on filtered air from exposure termination at week 22 until the end of the studies. Ten males and 10 females per

group were evaluated at 3 months. 3-Month Interim Evaluation: Exposure to indium phosphide for 3 months caused a microcytic erythrocytosis and also caused enlarged lungs and lesions in the respiratory tract and lung-associated lymph nodes. Although qualitatively similar to those observed in the 14-week studies, these effects were considerably less severe. However, the lesions in the lungs of rats exposed to 0.1 or 0.3 mg/m³ were considered sufficiently severe that exposure was discontinued in these groups, and the groups were allowed to continue unexposed for the remainder of the study. Survival, Body Weights, and Clinical Findings: Exposure to indium phosphide had no effect on survival or body weight gain. During the last 6 months of the study, rats in the 0.03 and 0.3 mg/m³ groups became lethargic and males breathed abnormally. Pathology Findings: At 2 years, exposure to indium phosphide caused increased incidences of alveolar/bronchiolar adenomas and carcinomas in rats. Squamous cell carcinoma of the lung occurred in four male rats exposed to 0.3 mg/m³. As observed in the 14-week study and at the 3-month interim evaluation, a spectrum of inflammatory and proliferative lesions of the lung were observed in all exposed groups of males and females; however, the extent and severity of the lesions were generally greater and included atypical hyperplasia, chronic inflammation, alveolar epithelial hyperplasia and metaplasia, alveolar proteinosis, and interstitial fibrosis. Exposure to indium phosphide also caused increased incidences of benign and malignant pheochromocytomas of the adrenal gland in males and females. Marginal increases in the incidences of mononuclear cell leukemia in males and females, fibroma of the skin in males, and carcinoma of the mammary gland in females may have been related to exposure to indium phosphide. 2-YEAR STUDY IN MICE: Groups of 60 male and 60 female mice were exposed to particulate aerosols of indium phosphide at concentrations of 0, 0.03, 0.1, or 0.3 mg/m³, 6 hours per day, 5 days per week, for 21 weeks (0.1 and 0.3 mg/m³ groups) or 105 weeks (0 and 0.03 mg/m³ groups). Animals in the 0.1 and 0.3 mg/m³ groups were maintained on filtered air from exposure termination at week 21 until the end of the studies. Ten males and 10 females per group were evaluated at 3 months. 3-Month Interim Evaluation: Exposure to indium phosphide for 3 months affected the circulating erythroid mass and caused enlarged lungs and lesions in the respiratory tract and lung-associated lymph nodes. These effects, although qualitatively similar to those observed in the 14-week studies, were considerably less severe. However, the lesions in the lungs of mice exposed to 0.1 mg/m³ and greater were considered sufficiently severe that exposure was discontinued in these groups and the groups were allowed to continue unexposed for the remainder of the study. Survival and Body Weights: In general, exposure to indium phosphide for 2 years reduced survival and body weight gain in exposed males and females. Pathology Findings: At 2 years, exposure to indium phosphide caused increased incidences of alveolar/bronchiolar carcinomas in males and alveolar/bronchiolar adenomas and carcinomas in females. In addition to the alveolar proteinosis and chronic active inflammation seen at earlier time points, serosa fibrosis and pleural mesothelial hyperplasia were also present. The incidences of hepatocellular neoplasms were also significantly increased in exposed males and females. Exposed groups of males and females had increased incidences of eosinophilic foci of the liver at 2 years. Marginal increases in the incidences of neoplasms of the small intestines in male mice may have been related to exposure to indium phosphide. Exposure to indium phosphide also caused inflammation of the arteries of the heart, primarily the coronary arteries and the proximal aorta, and to a lesser extent the lung-associated lymph nodes in males and in females. TISSUE BURDEN ANALYSES: Deposition and clearance studies of indium following long term exposure of rats and mice to indium phosphide by inhalation were performed. Although there were quantitative differences in lung burden and kinetic parameters for rats and mice, qualitatively they were similar. Deposition of indium in the lungs appeared to follow a zero-order (constant rate) process. Retained lung burdens throughout the studies were proportional to exposure concentration and duration. No differences in elimination rates of indium from the lungs were observed as a function of exposure concentration in either rats or mice. These studies indicated that elimination of indium was quite slow. Mice exhibited clearance half-times of 144 and 163 days for the 0.1 and 0.3 mg/m³ groups, respectively, as compared to 262 and 291 days for rats exposed to the same concentrations. The lung deposition and clearance model was used to estimate the total amount of indium deposited in the lungs of rats and mice after exposure to 0.03 mg/m³ for 2 years or to 0.1 or 0.3 mg/m³ for 21 or 22 weeks, the lung burdens at the end of the 2-year study, and the area under lung burden curves (AUC). For both species, estimates at the end of 2 years indicated that the lung burdens in the continuously exposed 0.03 mg/m³ groups were greater than those in the 0.1 or 0.3 mg/m³ groups. The lung burdens were lowest in the 0.1 mg/m³ groups. Because of the slow clearance of indium, the lung burdens in the 0.1 and 0.3 mg/m³ groups were approximately 25% of the maximum levels in rats and 8% in mice approximately 83 weeks after exposure was stopped. The AUCs and the total amount of indium deposited per lung at the time exposure was stopped indicate that the 0.3 mg/m³ groups were exposed to a greater amount of indium phosphide than were the 0.03 or 0.1 mg/m³ groups, with the 0.1 mg/m³ group receiving the lowest exposure. In rats and mice, the second-year AUC for the 0.03 mg/m³ group was equivalent to that of the 0.3 mg/m³ group. Regardless of how the total dose of indium to the lung was estimated, total exposure to indium in the 0.1 mg/m³ groups was less than that in the other two groups implying that in these studies, 0.1 mg/m³ may be considered the low dose. GENETIC TOXICOLOGY: No significant increases in the frequencies of micronucleated normochromatic erythrocytes were noted in peripheral blood samples of male or female mice exposed to indium phosphide for 14 weeks. Although there was a significant increase in micronucleated polychromatic erythrocytes in 30 mg/m³ male mice, there was no increase in female mice, and the percentage of polychromatic erythrocytes was not altered in males or females. CONCLUSIONS: Under the conditions of these 2-year inhalation studies, there was clear evidence of carcinogenic activity of indium phosphide in male and female F344/N rats based on increased incidences of benign and malignant neoplasms of the lung. Increased incidences of **pheo-chromocytoma** of the adrenal medulla in males and females were also considered to be exposure related. Marginal increases in incidences of mononuclear cell leukemia in males and females, fibroma of the skin in males, and carcinoma of the mammary gland in females may

have been related to exposure to indium phosphide. There was clear evidence of carcinogenic activity of indium phosphide in male B6C3F1 mice based on increased incidences of malignant neoplasms of the lung and benign and malignant neoplasms of the liver. Marginal increases in incidences of adenoma and carcinoma of the small intestine may have been related to exposure to indium phosphide. There was clear evidence of carcinogenic activity of indium phosphide in female B6C3F1 mice based on increased incidences of benign and malignant neoplasms of the lung. Increased incidences of liver neoplasms in females were also considered to be exposure related. Exposure to indium phosphide by inhalation resulted in nonneoplastic lesions in the lung of male and female rats and mice, the adrenal medulla of female rats, and the liver and heart of male and female mice.

PMID: 12087422 [PubMed - as supplied by publisher]

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PHTHALATES

Phthalates are chemicals used to make plastics flexible and they have been implicated in causing premature breast development in girls, which is a condition called thelarche. There has been an epidemic of thelarche on the island of Puerto Rico for the last two decades where affected girls begin breast development between the ages of 6 and 24 months. Researchers have finally concluded that the cause is phthalates. There is some indication that phthalates may also affect thyroid function.

Panel Expresses Concern About DEHP, A Plasticizer, As Used In Medical Devices For Ill Newborns

After a 15-month review of safety data on seven phthalates, or plasticizers -- the chemicals used to give plastics such characteristics as flexibility and strength -- an expert panel set up by the NIEHS/NTP's [Center for the Evaluation of Risks on Human Reproduction](#), has expressed "serious concern" about the use of one of the chemicals, DEHP, to make polyvinyl chloride (PVC) medical tubing and other medical devices for feeding and medicating critically ill newborn infants. Panel members said they hoped their finding would spur industry to find a substitute material but that, at this time, DEHP-derived PVC tubing continues to be needed to support preemies and other ill newborns through life-and-death situations.

The panel, which was formed of outside and government experts, including several from the [National Institute of Environmental Health Sciences](#) and the [National Toxicology Program](#) and a chair from the [Environmental Protection Agency](#), said DEHP could leach from continuously used tubing in sufficient amount to possibly affect the development of the male infant's reproductive system. DEHP is no longer used in toys intended for mouthing - nipples, teething, pacifiers, rattles - by U.S. manufacturers. Soft PVC teething toys have also been banned by the European Union.

The panel, working over a 15-month period, reviewed data on seven plasticizers and generally found "minimal" or "negligible" concerns about the others. A backgrounder on the panel's work is available at <http://ntp-server.niehs.nih.gov/htdocs/liason/CERHRPhthalatesAnnct.html>

The following study shows that long-term (3 months) treatment of rats with phthalates causes "changes are consistent with persistent hyperactivity in the gland." What this means is that exposure of foods or waters to flexible plastics (water containers, plastic wrap, etc.) could be a cause of hyperthyroidism. Also, note that fat lowering drugs like clofibrate and fenofibrate can have the same effects.

Toxicol Lett 1988 Jan;40(1):37-46

Alterations in the thyroids of rats treated for long periods with di-(2-ethylhexyl) phthalate or with hypolipidaemic agents.

Price SC, Chescoe D, Grasso P, Wright M, Hinton RH

Robens Institute of Industrial and Environmental Health and Safety, University of Surrey, Guildford, U.K.

Treatment of rats for periods of 3 months or longer with the hypolipidaemic drugs clofibrate and fenofibrate or with the plasticiser di-(2-ethylhexyl) phthalate causes alterations in the thyroid. The colloid is shrunken and contains calcium-rich inclusions. Electron microscopy shows increases in the number and size of lysosomes, hypertrophy of the Golgi apparatus and dilation of the rough endoplasmic reticulum. These changes are consistent with persistent hyperactivity in the gland.

Environ Health Perspect 1986 Dec;70:195-210

Effects of phthalic acid esters on the liver and thyroid.

Hinton RH, Mitchell FE, Mann A, Chescoe D, Price SC, Nunn A, Grasso P, Bridges JW

The effects, over periods from 3 days to 9 months of administration, of diets containing di-2-ethylhexyl phthalate are very similar to those observed in rats administered diets containing hypolipidemic drugs such as clofibrate. Changes occur in a characteristic order commencing with alterations in the distribution of lipid within the liver, quickly followed by proliferation of hepatic peroxisomes and induction of the specialized P-450 isoenzyme(s) catalyzing omega oxidation of fatty acids. There follows a phase of mild liver damage indicated by induction of glucose-6-phosphatase activity and a loss of glycogen, eventually leading to the formation of enlarged lysosomes through autophagy and the accumulation of lipofuscin. Associated changes are found in the kidney and thyroid. The renal changes are limited to the proximal convoluted tubules and are generally similar to changes found in the liver. The effects on the thyroid are more marked. Although the levels of thyroxine in plasma fall to about half normal values, serum triiodothyronine remains close to normal values while the appearance of the thyroid varies, very marked hyperactivity being noted 7 days after commencement of treatment, this is less marked at 14 days, but even after 9 months treatment there is clear

cut evidence for hyperactivity with colloid changes which indicate this has persisted for some time. Straight chain analogs of di-2-ethylhexyl phthalate, di-n-hexyl phthalate and di-n-octyl phthalate differ entirely in their short-term effects on the liver and kidney but have similar effects on the thyroid. The short-term in vivo hepatic effects of the three phthalate esters can be reproduced in hepatocytes in tissue culture. All three phthalate esters, as well as clofibrate, have early marked effects on the metabolism of fatty acids in isolated hepatocytes. The nature of these changes is such as to increase storage of lipid in the liver. A hypothesis is presented to explain the progress from these initial metabolic effects to the final formation of liver tumors.

Comp Biochem Physiol C Pharmacol Toxicol Endocrinol 1995 Jun;111(2):317-23

Hypolipidemic agents alter hepatic mitochondrial respiration in vitro.

Chance DS, McIntosh MK

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The direct effects of three different classes of structurally diverse hypolipidemic agents on respiration were studied in mitochondria isolated from donor Sprague-Dawley rats. Two classes of peroxisome proliferators (i.e. plasticizers and hypolipidemic hormones and drugs) and one class of peroxisome inhibitors (i.e. anti-psychotic drugs) were studied. The phthalate ester plasticizers dibutylphthalate, ethylhexanoic acid and di(2-ethylhexyl) adipate, the hypolipidemic hormones or drugs dehydro-epiandrosterone (DHEA), thyroxine (T4), triiodothyronine (T3), gemfibrozil, clofibrate and naphthoflavone, and the anti-psychotic drugs chlorpromazine, thioridazine and fluphenazine were studied. As the dose of the plasticizer dibutylphthalate increased from 8 to 200 $\mu\text{mol/l}$, there was a decrease ($P < 0.05$) in state 3 (+ADP) respiration and in the respiratory control ratio for both substrates tested. The anti-psychotic drug chlorpromazine decreased state 3 malate + pyruvate-supported respiration and increased state 3 succinate-supported respiration. As the concentration of all three anti-psychotic drugs increased, there was a linear increase in state 4 respiration (-ADP) and a decrease in the respiratory control ratio for both substrates tested. As the dose of the hypolipidemic agents DHEA, gemfibrozil and T4 increased, there was a linear reduction in state 3 malate + pyruvate-supported respiration. However, when succinate was used as the substrate to support respiration, only the thyroid hormones significantly decreased state 3 respiration. Gemfibrozil, T4 and T3 increased state 4 respiration, regardless of the substrate used. As the dose of clofibrate, gemfibrozil, and the thyroid hormones increased, there was a linear reduction in the respiratory control ratio for both substrates tested.

Nail Polish and Other Cosmetics May Cause Infertility

From Dr. Mercola's website, mercola.com

Women of reproductive age should avoid using certain nail polishes, perfumes, and hair sprays containing an ingredient known to cause lifelong reproductive impairments in male rats, [The Environmental Working Group](#), an environmental advocacy group, is cautioning.

The ingredients in question are **dibutyl phthalates (DBP)** industrial chemicals that are used as plastic softeners and solvents in a wide variety of products such as:

- **Nail Polish**
- **Perfume**
- **Hair Spray**
- **Toys**
- **Detergents**
- **Food packages**

The warning was based in large part on a recently completed CDC study ([Environ Health Perspect 2000 Oct;108:972-82](#)), in which the investigators found levels of the metabolized compound in women of childbearing age.

"Women of reproductive age (20-40 years) were found to have significantly higher levels of monobutyl phthalate, a reproductive and developmental toxicant in rodents, than other age/gender groups. From a public health perspective, these data provide evidence that phthalate exposure is both higher and more common than previously suspected," the CDC investigators wrote.

The investigators also speculated that the higher levels in women of reproductive age were due to the use of cosmetics such as perfume, nail polishes, and hair sprays. The extensive use of these products among women is probably leading to the **inhalation and absorption of this chemical through the lungs**, the investigators said.

The report from the Environmental Working Group (EWG) (LINK) entitled "Beauty Secrets" suggests that the substance may be responsible for the following problems, which have increased during the 1970s and '80s:

- **Declining sperm counts**
- **Increase in sexual deformities**
- **Increase in testicular cancer**

The EWG says that getting any immediate regulatory action passed is virtually impossible, due to the fact that the associations are difficult to impossible to prove. Under the current regulations, **the responsibility of proving that there is a public health threat from cosmetics primarily falls upon US health authorities rather than the manufacturers.**

Phthalate Plasticizers Dangerous, Especially to Children

Many of the chemicals in various plastics, especially PVC, can be harmful to children, according to several new reports. Certain chemicals known as **phthalates** are used as plasticizers, which serve to make the plastic more flexible. Below are 2 recent studies showing dangers of 2 different types of phthalates.

DEHP

Although research is currently ongoing on the toxicity of plasticizers that are commonly blended with PVC products, Italian researchers fear that they may pose a danger to babies.

In a recently published review of existing studies, Dr. Giuseppe Latini, a Pediatrician, notes some interesting points concerning the most common plasticizer, di-(2-ethylhexyl)-phthalate (DEHP):

- **Many plastic items are made of polyvinylchloride (PVC) blended with plasticizers**, with DEHP being the most frequently used.
- **DEHP migrates at a constant rate from plastics to the environment.**
- **It has been detected in water, soil and food and is therefore considered as a widespread environmental contaminant.**
- **Over the past several years, a number of publications concerning toxic effects of DEHP on animals and humans have been reported**

Dr. Latini notes that "long-term exposure, especially in human beings at risk such as pregnant women and children, requires more in-depth studies."

He concludes that if future studies confirm the dangers of DEHP, "it would be advisable in the future to replace current PVC plasticizers, especially if they come into contact with babies, with better-quality materials."

BBP

DEHP is not the only plasticizer or phthalate to show toxic effects. **Butyl benzyl phthalate (BBP)**, another plasticizer, has been shown to have **estrogenic qualities**, have **toxic effects on the testicles**, and to **cause birth defects**.

Now, researchers from Japan have found that the toxic effects of BBP exposure can extend into the next generation, at least in lab animals.

Investigators found that oral doses of BBP in rats had the following effects:

In the parent animals:

- Increase in **kidney** weight in rats (both sexes)
- Increase in **liver** weight (males)
- Decrease in the weight of the **ovaries** (females)
- Decrease in body weight gain (males)
- Decrease in **testosterone** levels
- Increase in **follicle stimulating hormone (FSH)**

In the offspring:

- **Decreased body weight**
- **Decreased anogenital distance** (AGD), or the distance from genital tubercle to the anus, in males
- **Increased AGD** in females
- **Genital development** of male fetuses was delayed
- Macroscopic and microscopic **changes of the testes** in males
- **Decreased serum concentrations of testosterone** in males

Biology of the Neonate November, 2000; 78: 269-276 and Reproductive Toxicology 2000 Nov 1; 14: 513-532

DR. MERCOLA'S COMMENT: The effects of these chemicals on the endocrine system, particularly during pregnancy, breastfeeding and childhood are very disturbing. I would strongly disagree with the author of the first study who says that if future studies confirm the dangers of these plasticizers, that they should be replaced by safer substances.

It is **criminal** to wait for further results while people continue to be exposed. The precautionary principle dictates that pregnant women and babies should not be exposed to substances unless they have been shown to be essentially safe. The burden of proof should be on the manufacturers of these chemicals to **PROVE** that they are safe and should **NOT** be on scientists to prove that it is toxic.

About a year ago the European Union (EU) has banned phthalates from toys intended for children under 3 years of age (Lancet, Dec 11, 1999).

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POTASSIUM

POTASSIUM AND THYROID DISEASE

Studies show that potassium becomes very deficient in the hyperthyroid state. It can become so deficient that hypokalemic paralysis results. This is a condition in which the whole body becomes rigid because of potassium deficiency. There are reports in the literature of people found in a state of hypokalemic paralysis in the street. When they are taken to the hospital and revived with potassium infusions, they are often found to have hyperthyroidism. For an unknown reason this occurs at a higher rate among Asians. It may be genetic or dietetic (high sodium intake from soy sauce, perhaps??). There are indications that potassium deficiency may also be involved in hyperthyroidism and the rapid weight gain of hypos may be the result of potassium deficiency.

The four minerals, sodium, potassium, calcium, and magnesium are next to each other in the Periodic Table and form a square on the left side. There are strong interactions between these four minerals. The balances between these four minerals seems to be critical to health and are probably very critical for thyroid health. Excess amounts or deficiencies of any one of the four may severely disrupt thyroid function. Additionally there seem to be interactions between these four minerals and copper and zinc, which are two metallic minerals with critical thyroid functions. It seems that a copper deficiency interferes with the proper functioning of both potassium and magnesium, and zinc seems more related to sodium and calcium metabolism. Also all of these minerals seem involved in either the production, degradation, or cellular response to thyroid hormone.

Potassium, sodium, and lithium are alkaline minerals which are involved in the cellular pumps which regulate the transport of water and nutrients through the cell walls. There is evidence that a potassium deficiency can cause the cells to fill with water leading to an overall edema in the body. It's possible that edema of the brain cells from potassium deficiency may be involved in chronic headaches. It's also possible that potassium deficiency is responsible for the rapid increase in body weight seen in thyroid patients. This increase in body weight seems to occur despite calorie restriction and may be the result of swelling of all the body's cells with water.

Indications of potassium deficiency include symptoms such as muscle weakness, which is a condition reported by many thyroid patients.

You will also see below that eating licorice can deplete potassium with possible fatal consequences. I would strongly urge anyone with thyroid disease to not eat licorice.

For these reasons I think studying potassium is critically important to understanding thyroid physiology.

GENERAL INFORMATION ABOUT POTASSIUM

From the book, "Healthy Healing" by Linda Rector Page:

"Potassium--an electrolyte mineral located in body fluids. Potassium balances the acid/alkaline system, transmits electrical signals between cells and nerves, and enhances athletic performance. It works with sodium to regulate the body's water balance, and is necessary for heart health against hypertension and stroke, (people who take high blood pressure medication are vulnerable to potassium deficiency), muscle function, energy storage, nerve stability, and enzyme and hormone production."

"Potassium helps oxygenate the brain for clear thinking and controls allergic reactions. Stress, hypoglycemia, diarrhea and acute anxiety or depression generally result in potassium deficiency. A potassium broth from vegetables is one of the greatest natural healing tools available for cleansing and restoring body energy. Good food and herb sources are fresh fruits, especially kiwis and bananas, potatoes, sea vegetables, spices like coriander, cumin, basil, parsley, ginger, hot peppers, dill weed, tarragon, paprika, and tumeric, lean poultry and fish, dairy foods, legumes, seeds, and whole grains."

From the Nutrition Almanac by Kirschmann (excerpts): "...Potassium constitutes 5% of the total mineral content of the body...Potassium and sodium help regulate water balance within the body (potassium crosses over more easily); that is, they help regulate the distribution of fluids on either side of the cell walls and preserve proper alkalinity of the body fluids. Potassium also regulates the transfer of nutrients to the cells. ..."

"Potassium is necessary for normal growth enzymatic reactions. It unites with phosphorus to send oxygen to the brain and also functions with calcium in the regulation of neuromuscular activity. The synthesis of muscle protein and protein from amino acids in the blood requires potassium, as does the synthesis of nucleic acids. It aids in keeping skin healthy and in keeping a stable blood pressure."

"Potassium assists in the conversion of glucose to the form in which this substance can be stored in the liver as glycogen, and then to its useful form to do the body's work. Protein and carbohydrate metabolism are dependent upon potassium. It stimulates the kidneys to eliminate poisonous body wastes. Potassium works with sodium to help normalize the heartbeat."

STUDIES ON POTASSIUM DEFICIENCY AND THYROID CONDITIONS

The following study indicates that potassium levels are low in patients with hyperthyroidism, muscular weakness is proportionate to potassium deficiency, and correction of thyroid hormone levels results in correction of potassium levels.

Rev Neurol 1999 Sep 16-30;29(6):510-2

Title: Total body *potassium* in relation to thyroid hormones and hyperthyroidism.

Author

Edmonds CJ; Smith T

Source

Clin Sci, 60(3):311-8 1981 Mar

Abstract

1. Body weight and total body *potassium* were measured in 23 hyperthyroid patients before and at various stages during treatment and in 19 athyretic patients who were being treated with high-dose L-thyroxine. 2. **In the hyperthyroid patients the total body potassium rose by 23 +/- 2.8% (SEM) within a few weeks of restoring the blood thyroid hormone levels to normal.** The body *potassium* values after treatment were close to that expected in these individuals if they were healthy indicating that a considerable loss of body *potassium* is usual in hyperthyroidism. 3. The gain of total body *potassium* in hyperthyroidism averaged 71 +/- 8 mmol for each kg of body weight gained (compared with muscle *potassium* concentration of about 92 mmol/kg). In contrast, weight loss produced by dietary treatment of obesity caused very little change of body *potassium* (maximum averaged was 14 +/- 4 mmol/kg wt. loss). 4. **Among the patients with hyperthyroidism, the greatest muscular weakness was present in those with the greatest body potassium loss** and these patients regained a large amount of *potassium* relative to weight on recovery. 5. **Total body potassium changes were closely related to total plasma tri-iodothyronine concentrations but unrelated to the thyroxine levels.**

The following study indicates that hyperthyroidism may be the result of potassium deficiency which may be caused or increased by physical exercise or ingestion of carbohydrates.

[No title available].

[Article in Spanish]

Carod-Artal FJ, Delgado-Villora R

Programa de Neuroclinica, Hospital Sarah, Red de Hospitales del Aparato Locomotor, Brasilia DF, Brasil. javier@bsb.sarah.br

[Medline record in process]

INTRODUCTION: Thyrotoxic hypokalemic periodic paralysis is characterized by recurrent episodes of motor weakness of variable intensity associated with thyroid overactivity. It is usually associated with low plasma potassium levels and is often precipitated by physical activity or ingestion of carbohydrates. **CLINICAL CASES:** We describe two men, aged 33 and 50, who complained of several episodes of muscular paralysis in the context of previously undiagnosed hyperthyroidism and associated with low plasma potassium levels. There were clearly raised levels of T3, T4 and free T4 and TSH was depressed due to hyperactive diffuse goitre. **In one patient the precipitating factor was known to have been a large intake of carbohydrates and intense physical exercise.** Antithyroid treatment, and the resulting correction of hyperthyroid function, prevented any further episodes of muscular weakness in both patients. **CONCLUSIONS:** Thyrotoxic periodic paralysis should be considered in the differential diagnosis of all acute episodes of motor paralysis in young patients. Determination of the plasma levels of potassium and thyroid hormones helps diagnosis. Early diagnosis is important so as to be able to establish antithyroid treatment and avoid further episodes of weakness.

This study shows that potassium deficiency alters the physiology of thyroid hormone activity.

Title

Potassium deficiency enhances the effect of *thyroid* hormone on NaK-ATPase in liver and kidney.

Author

Shishiba Y; Ozawa Y; Takaishi M; Eguchi N; Shimizu T

Source

Endocrinol Jpn, 27(3):329-36 1980 Jun

Abstract

In order to examine the possibility that the changes in electrolytes in tissue alter the effect of *thyroid* hormone on NaK-ATPase, rats were fed either synthetic K-deficient diet or synthetic K-normal diet. K-deficient diet induced a reduction in K content in serum or kidney, while that of the liver remained unchanged. **When a daily dose of 2.5 micrograms T3 was administered for 7 days to K-deficient rats, both Mg- and NaK-ATPase of the homogenate of liver and kidney were elevated, while the same dose failed to influence those enzymes in K-normal rats.** Furthermore, T3 dose increased the Na content of liver and kidney in K-deficient rats, resulting in a significant decrease in the K/Na ratio in those tissue. Based on the estimation from chloride space, the decrease in K/Na was deemed to have occurred mainly in the intracellular space. **As the levels of serum thyroid hormone and liver T3 were not influenced by K-deficiency, the effect of K depletion is likely to be mediated not through the alteration in thyroid hormone kinetics, but through some other mechanism such as the elevation of intracellular Na.** The present study demonstrates that K deficiency may sensitize NaK-ATPase to the effect of *thyroid* hormone.

HYPOKALEMIC PARALYSIS

Title

Hypokalemic paralyses: a review of the etiologies, pathophysiology, presentation, and therapy.

Author

Stedwell RE; Allen KM; Binder LS

Address

Department of Emergency Medicine, Texas Tech University Health Sciences Center, El Paso 79905.

Source

Am J Emerg Med, 10(2):143-8 1992 Mar

Abstract

Acute hypokalemic paralysis is an uncommon cause of acute weakness. Morbidity and mortality associated with unrecognized disease include respiratory failure and death. Hence, it is imperative for physicians to be knowledgeable about the causes of hypokalemic paralysis, and consider them diagnostically. The hypokalemic paralyses represent a heterogeneous group of disorders with a final common pathway presenting as acute weakness and hypokalemia. Most cases are due to familial hypokalemic paralysis; however, sporadic cases are associated with **diverse underlying etiologies including thyrotoxic periodic paralysis, barium poisoning, renal tubular acidosis, primary hyperaldosteronism, licorice ingestion, and gastrointestinal potassium losses.** The approach to the patient with hypokalemic paralysis includes a vigorous search for the underlying etiology and potassium replacement therapy. Further therapy depends on the etiology of the hypokalemia. Disposition depends on severity of symptoms, degree of hypokalemia, and chronicity of disease.

Title: Periodic paralysis and the sodium-potassium pump.

Author: Layzer RB

Source: Ann Neurol, 11(6):547-52 1982 Jun

Abstract

Analysis of the pathophysiology of hypokalemic paralysis, as it occurs in **barium** poisoning, chronic potassium deficiency, and thyrotoxicosis, suggests that these disorders may have a similar mechanism. An increased ratio of muscle sodium permeability to potassium permeability reduces the ionic diffusion potential, while the resting membrane potential is sustained by an increase of Na-K pump electrogenesis. The result is that potassium entry (the sum of active and passive influx) exceeds potassium efflux; this causes a large shift of extracellular potassium into muscle until the Na-K pump turns off, leading to depolarization and paralysis. The primary defect in familial hypokalemic periodic paralysis, as in the example of **barium** poisoning, may be a marked reduction of muscle permeability to potassium.

The following study indicates symptoms of potassium deficiency induced by the consumption of licorice. The symptoms are muscular weakness and pain. The descriptions make me wonder if a potassium deficiency is involved in fibromyalgia.

Title

Glycyrrhizin (**licorice**)-induced hypokalemic myopathy. Report of 2 cases and review of the literature.

Author

Shintani S; Murase H; Tsukagoshi H; Shiigai T

Address

Department of Neurology, Toride Kyodo General Hospital, Ibaraki, Japan.

Source

Eur Neurol, 32(1):44-51 1992

Abstract

Fifty-nine cases of glycyrrhizin (**licorice**)-induced hypokalemic myopathy (GIHM), 2 females treated in our departments (85 and 73 years old) and 57 cases reported in the literature were studied, and conditions leading to the onset, factors, clinical manifestations, laboratory assessments, muscle biopsy findings, treatment and outcome were discussed. The 59 GIHM cases comprised 32 men, 25 women and 2 patients without record of sex; the average age was 55.2 years. In many cases, conditions leading to the onset of GIHM were **habitual licorice ingestion**, ingestion of antituberculosis agents containing **licorice** and long-term ingestion of **licorice**-containing agents for chronic gastritis, chronic hepatitis or chronic dermatitis. The combined use of hypotensive diuretic agents increased the risk of GIHM in an overwhelming number of cases. The main clinical symptom was **flaccid quadriplegia** in almost all cases, with **muscle pain** in 32.2% and peripheral dysesthesia in the extremities, manifested mainly by numbness (27.1%). Laboratory findings included a mean serum K⁺ value of 1.98 mEq/l (56 GIHM cases), a mean creatine kinase of 5,385.7 IU/l (n = 30), a mean blood aldosterone concentration of 2.92 ng/dl (n = 30; normal: 2.0-13.0 ng/dl) and a mean plasma renin activity of 0.17 ng/ml/h (n = 27; normal: 0.8-4.4 ng/ml/h). Muscle biopsy was performed in 17 of the 59 cases with resultant findings of myopathic changes consisting mainly of phagocytosis, necrotic fibers, vacuolar degeneration, together with sporadic neurogenic changes. **Complete cure was attained in 57 of the 59 cases of GIHM by discontinued ingestion of glycyrrhizin (licorice) and potassium supplement.**

POTASSIUM INTERACTIONS WITH MAGNESIUM

The following study indicates that a magnesium deficiency decreases the activity of the sodium-potassium cellular pumps. "It is suggested that this leads to an increase in intracellular Na⁺, resulting in a change in the membrane potential, and may contribute to the arrhythmias associated with magnesium deficiency." Thus magnesium deficiency may be causing irregular heart beat by its effect on the sodium-potassium pumps.

Title

Effects of dietary magnesium on sodium-potassium pump action in the heart of rats.

Author

Fischer PW; Giroux A

Address

Nutrition Research Division, Health and Welfare Canada, Ottawa, Ontario.

Source

J Nutr, 117(12):2091-5 1987 Dec

Abstract

Sprague-Dawley rats were fed a basal AIN-76 diet containing 80, 200, 350, 500 or 650 mg of magnesium per kilogram of diet for 6 wk. Ventricular slices, as well as microsomal fractions, were prepared from the hearts and were used to determine sodium-potassium pump activity. Sodium-potassium pump activity was assessed in the microsomal membranes by determining the ouabain-inhibitable Na⁺, K⁺-ATPase activity and [3H]ouabain binding, and in the ventricular slices, by determining ouabain-sensitive 86Rb uptake under K⁺-free conditions. The ATPase activity increased with increasing dietary magnesium, so that in the hearts of those animals that were fed 500 and 650 mg of magnesium/kg diet, it was significantly greater than the activity in the hearts of the animals fed 80 and 200 mg/kg diet. Similarly, 86Rb uptake by heart slices from rats fed 500 and 650 mg of magnesium/kg diet was significantly greater than the uptake by heart slices from animals fed 80 and 200 mg/kg diet. [3H]Ouabain binding did not change with increasing dietary magnesium. **Thus, magnesium deficiency appears to have no effect on the number of sodium-potassium pump sites, but does decrease the activity of the pump. It is suggested that this leads to an increase in intracellular Na⁺, resulting in a change in the membrane potential, and may contribute to the arrhythmias associated with magnesium deficiency.**

Rubidium and Cesium are alkaline minerals located below potassium on the Periodic Table. There is evidence that excessive amounts of these minerals can deplete potassium. Because they are heavier minerals, it is expected that cesium and rubidium have longer half-life times in the body and very small amounts may have significant effects on potassium.

Title

Ion effects on gating of the Ca(2+)-activated K⁺ channel correlate with occupancy of the pore.

Author

Demo SD; Yellen G

Address

Howard Hughes Medical Institute, Johns Hopkins University School of Medicine, Baltimore, Maryland 21205.

Source

Biophys J, 61(3):639-48 1992 Mar

Abstract

We studied the effects of permeant ions on the gating of the large conductance Ca(2+)-activated K⁺ channel from rat skeletal muscle. Rb⁺ blockade of inward K⁺ current caused an increase in the open probability as though Rb⁺ occupancy of the pore interferes with channel closing. In support of this hypothesis, we directly measured the occupancy of the pore by the impermeant ion Cs⁺ and found that it strongly correlates with its effect on gating. This is consistent with the "foot-in-the-door model of gating, which states that channels cannot close with an ion in the pore. However, because Rb⁺ and Cs⁺ not only slow the closing rate (as predicted by the model), but also speed the opening rate, our results are more consistent with a modified version of the model in which the channel can indeed close while occupied, but the occupancy destabilizes the closed state. Increasing the occupancy of the pore by the addition of other permeant (K⁺ and Tl⁺) and impermeant (tetraethylammonium) ions did not affect the open probability. To account for this disparity, we used a two-site permeation model in which only one of the sites influenced gating. Occupancy of this "gating site interferes with channel closing and hastens opening. Ions that directly or indirectly increase the occupancy of this site will increase the open probability.

Title

Effect of diet upon the erythrocyte Na,K pump.

Author

DeLuise M; Izumo H; Grace EE; Flier JS

Source

J Clin Endocrinol Metab, 56(4):739-43 1983 Apr

Abstract

The number of erythrocyte Na,K-ATPase pump units has been found to be reduced in some populations of obese humans, but the effect of dietary factors upon the status of the erythrocyte pump has not been delineated. We have measured the number of Na,K-ATPase pump units by [3H]ouabain binding and the activity of the pump by ouabain-inhibitable 86rubidium uptake in response to nutritional maneuvers in several patient groups. There was no consistent change in the number or activity of Na,K-ATPase units in response to 1) an acute 600-cal meal, 2) a 3-day fast or refeeding after a fast in normal weight or obese subjects, 3) 2 weeks of hypocaloric (600 cal) feeding in obese subjects. Individuals with anorexia nervosa were also not significantly different from age- and sex-matched control subjects with respect to the erythrocyte Na,K pump. It is concluded that the circulating erythrocyte does not regulate the number or activity of Na,K pump units in response to short or medium term nutritional maneuvers. Differences between obese and thin populations with respect to the Na,K pump are not likely to be secondary to nutritional differences between the two groups.

Title

Analysis of the effects of *cesium* ions on potassium channel currents in biological membranes.

Author

Clay JR; Shlesinger MF

Source

J Theor Biol, 107(2):189-201 1984 Mar 21

Abstract

Cesium ions block potassium channels in biological membranes in a voltage dependent manner. For example, external*cesium* blocks inward current with little or no effect on outward current. Consequently, it produces a characteristic N-shaped current-voltage relationship. We have modeled this result by single file diffusion of ions in a narrow channel spanning the membrane with a special blocking site in the channel for *cesium* ions. The model enables us to make detailed comparisons of the effects of*cesium* on potassium channels in different types of biological membranes.

Title

Relationship between turnover of *cesium*-137 and dietary potassium content in potassium-restricted mice.

Author

Sato I; Matsusaka N; Tsuda S; Kobayashi H; Nishimura Y

Address

Faculty of Agriculture, Iwate University, Morioka, Japan.

Source

Radiat Res, 148(1):98-100 1997 Jul

Abstract

The biological half-life of ¹³⁷Cs and its organ distribution were investigated in mice fed various potassium-deficient diets. The biological half-life, which was 6.1 days in mice receiving the normal level of potassium, became longer as the dietary potassium content decreased, and ¹³⁷Cs was hardly excreted from the body when dietary potassium content was restricted to 200 mg/kg or less. The muscle showed the highest concentration of ¹³⁷Cs in both mice that had sufficient amounts of potassium and those that were potassium-deficient. Clearance of ¹³⁷Cs from tissues was generally suppressed when mice were fed a potassium-deficient diet, but the relative distribution pattern of ¹³⁷Cs was not affected by dietary potassium content. These results suggest that dietary potassium intake, which may vary with eating habits, affects the biological half-life of ¹³⁷Cs in humans.

ARTHRITIS as a CHRONIC POTASSIUM DEFICIENCY, chapter I

by Charles Weber

This site introduces a discussion of potassium nutrition and physiology especially as pertaining to rheumatoid arthritis.

OTHER CONTENTS [II. Arthritis Research](#) -- [III. Arthritis and Potassium](#) -- [IV. Roles of Potassium in the Body](#) -- [V. Electrolyte regulation \(sodium and potassium\)](#) -- [VI. Purpose of cortisol](#) -- [VII. Copper nutrition and physiology](#) - [VIII. Nutritional Requirements](#) -- [IX. Potassium in Foods](#) -- [X. Processing Losses](#) -- [X.cont. Losses in the kitchen](#) - [XI. Supplementation](#) -- [Side Effects and Heart Disease](#)

It is my contention that potassium deficiency is either causing, or greatly making worse, rheumatoid arthritis which I will shorten to "arthritis" in this article. In assessing the possibility of this hypothesis people have little to go on. Virtually any textbook in the past would devote no more than a paragraph to potassium which would state that potassium is never deficient in the diet, or give one exception to the dozen or more known, or in some only under clinical conditions.

The reason for this careless treatment of potassium is probably because potassium is present in almost all foods as grown in large quantities. Professionals think about it as if it were air or water. However even air and water can be deficient and if voluminous texts are not written on their deficiencies, it is because both deficiencies can be detected by our senses. Extremely powerful emotions and instincts impel people to correct these deficiencies immediately and at any cost. Potassium is odorless, colorless, and, in the usual concentrations, tasteless. There is no way to detect a deficiency and cell content can not even easily be assessed in the body by modern analytical procedures. Whole body cell content is virtually "invisible".

There is not any indication in the literature that potassium has ever been tried by scientists as an arthritis corrective. A rather exhaustive search of the medical literature has failed to disclose an experiment. This includes Excerpta Medica 1947 to 1974, and a computer search by the Central Library of the American Medical Association from 1965 back.

I will discuss potassium physiology and nutrition and what can be done to remove an actual deficiency and thus heal any tissue which has not actually been destroyed. If you do not know the meaning of a word in this article, for a definition click on <http://www.m-w.com> (Mirriam-Webster).

Please keep in mind, though, that potassium ramifies through every cell and process in the body, has no storage, and has a dangerous dependence on its precise control by nerve impulse transmission. This makes it a mineral to be cautious about. In particular I recommend getting as much as possible from food. Even food requires some care because it has a wide range of concentrations. You must take responsibility for your own intake and I assume no liability for the correctness of advice in this article. You use this information at your own risk.

Getting potassium from food is reasonably safe for normal people with reasonably sound kidneys. Even if you doubt my thesis of a connection between arthritis and potassium, you have nothing to lose by getting all the potassium that was originally in your food. It will even taste better. It will, in addition, help protect you from potassium's known link to heart disease. As the 12th century physician Maimonides expressed it: "A doctor should begin with simple treatments, trying to cure by diet before he administers drugs. No illness that can be treated by diet should be treated by any other means."

Anything a doctor can learn, you can also. There will be a list of definitions eventually which will make the difficult words much easier eventually. In the mean time one of the online technical dictionaries may do.

INTRODUCTION

Arthritis is the number one crippler in America. The estimate for rheumatoid arthritis is [43 million men, women and](#)

[children and at least 65 billion dollars lost each year currently](#). Two thirds of the victims are women, most of them over 45 [Rodman]. The terrible pains associated with arthritis, reminiscent of and similar to the medieval torture racks must surely be among the top causes of contemporary misery. These pains along with the actual physical disability, weak joints, and loss of energy which accompany them, cause an enormous loss of productivity, estimated to be over six billion dollars in 1978 [Arthritis Foundation]. Arthritis may be a considerable part of the cause of increasing welfare roles. Even industrial accidents are related to this monstrous and onerous burden that society carries. Small jolts and falls which should do little more than bring out some colorful language results in loss of hours and even months. It is more than just the loss of time itself. It is also the super caution that blocks even fairly healthy people from making fast, risky moves when they see some of the debacles their friends get into.

Nor is arthritis confined to North America. Countries at such extremes of latitude as Finland and Jamaica have even higher rates than we do [Kellgren]. The simple life is not any guarantee against misery either. The Masai tribesmen of Africa have high rates [Best p768]. Political or economic ideologies are not barriers. Arthritis crosses the iron curtain, is also present in nomadic hunters, and cave men, cave bears, and ancient Egyptians are thought to have had it [Bach][Crain]. It shows no obvious clear association with any culture even though it is very variable, with low rates in tribes near the Masai and Laplanders near the Finns in Finland, as well as insane people in Massachusetts {Allander p260}.

Most of the people who have pains in the joints have them because of arthritis. The pains usually strike first in the outer joints like fingers or joints with a history of injury. Load bearing joints are also vulnerable. The pain is most likely in the early morning. It is often accompanied by stiffness. It is not to be assumed that the disease is localized because the pain is, Arthritis is present throughout the body and can affect kidneys, pericardium of the heart, and connecting tissue [Strukov][Ropes]. It is a disease largely associated with humans [LaMont-Havers], probably partly because animals can not talk, but I suspect primarily because animals usually do not have access to refined food. Arthritis has few externally observable symptoms, especially in early stages. There are no known consistent biochemical changes in arthritis (which word in this article will be equated with "rheumatoid arthritis") except a much lower cellular potassium content than normal [LaCelle], and a higher [copper content](#) along with a protein which binds the copper in the serum [Schubert]. There has been an effort to use changes in some of the body's other proteins in diagnosis, but with limited success so far, although some of the other rheumatic diseases can be almost diagnosed from blood proteins alone [Waller]. As nearly as I can tell this seemed to be the consensus for arthritis at the 1982 Pan American Conference on Arthritis. There are significant correlations between IgM RF and IgA immune proteins and a higher disease activity [Chen] but the correlations are not perfect. C3 and C4 compliment are said to be the best of the other discriminators.[Sari, et al]. Arthritis sometimes has [fatigue](#) associated with it.

In the past arthritis was associated with old age in people's minds and there was a tendency to suffer it stoically as inevitable. While the medical profession has intellectually abandoned an assumption that only people in old age are affected, many laymen still assume this is the case. The concept that this is "old age" is pervasive, even creeping into common cultural media as modern as "Star Trek". This is not to indicate that the victims did not often attempt to do something. Arthritis has a long history of quack nostrums and screwball procedures. These quack remedies were assisted by the numerous spontaneous remissions that occur with arthritis or by pain deadening chemicals. It was not necessary to cure everyone, since those who were "cured" were very grateful and those who were not were fatalistic, since their doctors could do nothing either.

It is my contention that arthritis is either a potassium deficiency or is strongly affected by one. I suspect that some poison or some infections or decline in kidney function with age degrades our ability to concentrate potassium and thus makes it impossible to eat the food from which almost every processing procedure removes potassium these days. Arthritics characteristically have poor nourishment {Morgan et al}. One such poison which I suspect is the very poisonous bromine gas, since it probably affected me that way 50 years ago.

One technique which seemed to have some success was the use of spas. At least their popularity would seem to indicate some success. That king sized spa, the ocean, has been given credit for anti-arthritic tendencies also. This is plausible because the ocean contains potassium in about the same concentration as blood fluid. The spa at Bath, England, has a potassium content less than one tenth that of ocean water [Riley]. If it is typical of spas, then unless they were drinking the water, it is hard to see how it could have helped.

There have been closer associations with potassium. At one time sulfated potash was used to combat arthritis [Osol p1092]. It is not surprising that it fell into disfavor associated with such a poisonous anion. An anion is a negatively charged substance which neutralizes the positive charge of an ion like potassium. The first person to definitively link potassium to arthritis in no uncertain terms was DeCoti-Marsh in a book published in England in 1957 [deCoti-Marsh]. He claimed numerous case histories. He recommended a whole pot-pouri of anions to go with the potassium, some of them not nutritional, and some even poisonous. He attributed magical properties to these anions. His approach was reminiscent of the writings of ancient alchemists.

A more successful technique was the raw vegetable diet described by Holbrook in Europe during the forties [Holbrook]. This diet became quite popular, even though most people must have found it fairly unpalatable. Eppinger hinted that the success of this diet may have been due to its high potassium content [Eppinger]. It might have become more popular if a recommendation to use fried vegetables, soup, or to drink the boil water had been made, which would have permitted the same potassium intake. There have been experiments with vegetarian diets in recent years but they have been changed merely by removing meat from the diet which is probably why only moderate success has been attained.

At the present time there are several books relating diet to arthritis. Jarvis stresses honey and vinegar in his book [Jarvis]. Since honey is extremely low in potassium, it would be counter productive. The vinegar could be very

beneficial if well fed people are failing to metabolize all of the acetate ion because the acid hydrogen ion interferes with potassium at the excretion site as [will be developed later](#). I know of no tests reported in the literature testing this concept. Jarvis hints at other dietary changes also, which if followed, would increase potassium intake inadvertently.

Dong and Banks prescribe a diet free of chemicals, milk, meat and sugar, and low in fat [Dong]. If his diet were followed it would definitely increase potassium intake, especially since he stresses unprocessed vegetables. However, he attributes its success to freedom from allergens and chemicals, so that philosophically he tends to be in the same general physiological category as the autoimmune hypothesis is in, to be discussed later. I am fairly certain that those who have success with his diet do so because of the lucky quirk that potassium increases at the same time. I think a good case could be made for keeping chemicals out of food. Some, like sulfite which destroys vitamin B-1 are known to be harmful, some like dyes and nitrites are fraudulent and/or harmful. I doubt if removing them would have more than a small affect on arthritis though. Alexander recommends vitamin D against arthritis. However like Dong he also speaks of low sugar and raw vegetables [Alexander]. I doubt if the vitamin D had much affect on arthritis, although those using his diet must have had less trouble with tooth decay, tuberculosis, and rickets.

Allergy has been proposed as a possible cause but stressing allergens naturally present in food. It is quite conceivable that allergens damage the kidneys' ability to retain potassium. However, no one has established this yet. There is good evidence, though, of beneficial results from defeating allergy in specific cases.

Evidence from individual case histories and the known characteristics of potassium physiology supports the proposal that arthritis is either a potassium deficiency or that a deficiency is its most important symptom. The replete body contains about 75 times as much potassium or more as is usually in the processed diet, so if it is increased, it will still take quite awhile to come up to normal. However there should be satisfying initial results in a month or two or even less.

I have been almost alone in proposing potassium as being central to rheumatoid arthritis ([but see Dr. Jan de Vries' article](#)). However there is no substitute for an experiment, which has never been done. While you are waiting for such an experiment there is nothing stopping you from eating nutritious food and making sure you do not lose any of the potassium by your own preparations. I wish you good health.

Low potassium levels seem to occur more at night and in the hotter months of the year. This seems to coincide with the times when hypers have more hyperthyroid storms.

QJM 1996 Jun;89(6):463-8

Thyrotoxic periodic paralysis in a Chinese population.

Ko GT, Chow CC, Yeung VT, Chan HH, Li JK, Cockram CS

Department of Medicine, Chinese University of Hong Kong, Shatin.

We retrospectively evaluated the characteristics of adult patients admitted with thyrotoxic hypokalaemic periodic paralysis in Hong Kong. From 1984 to 1993, 45 Chinese adult patients were admitted with acute limb weakness, plasma potassium ≤ 3.5 mmol/l and thyrotoxicosis confirmed by laboratory investigations. All but one were male. Seventy-five percent of attacks occurred between 9pm and 9am. Half of the attacks occurred between July and October (49.1%), most commonly in August (20%). Mean (\pm SEM) plasma potassium on admission was 2.17 ± 0.08 mmol/l (range 1.1-3.5). In 15 episodes (27.3%), plasma potassium on recovery exceeded 5.0 mmol/l, while in three episodes (5.5%), potassium exceeded 6.0 mmol/l. No patient had a positive family history of thyrotoxic periodic paralysis. Only 28.9% had a known history of thyrotoxicosis before their first presentation with periodic paralysis. Twenty-seven (60%) had clinical evidence of thyrotoxicosis. Although all were biochemically thyrotoxic, 11.4% had only a mild degree of thyrotoxicosis (suppressed thyroid-stimulating hormone, high free thyroxine, but normal free triiodothyronine). One quarter of the patients had a normal erythrocyte zinc concentration, indicating either a short history of thyrotoxicosis or transient thyrotoxicosis. The diagnosis of thyrotoxic hypokalaemic paralysis should always be considered in Chinese patients with acute muscle weakness, especially in young males. Absence of clinical thyrotoxicosis does not exclude the diagnosis. Plasma potassium should be monitored carefully during treatment to prevent rebound hyperkalaemia.

Subj: Re: [hyperthyroidism] Recently diagnosed with hyperthyroidism [Canada]

Date: 2/20/01 10:01:36 AM Pacific Standard Time

From: Penny

Reply-to: hyperthyroidism@yahoogroups.com

To: hyperthyroidism@yahoogroups.com

John

I can't wait for the website to be repaired. I've been dying to talk to you about this potassium thing. Thanks, by the way, for your recent potassium article at the site.

Anyway, you know I'm hypo, and I'd also been feeling that potassium was something I needed to look into. Thanks to your research, I've been experimenting with approximately 1,000 mgs a day (more when I can manage it) and every time I do, I see a huge improvement in my strange heart sensations. However, I also KNOW that I'm deficient in magnesium, because of muscle twitching and spasms etc. so I'm still taking that as well. I just don't feel right if I don't take it. Does this make sense, to need both?

I'm definitely liking the effect of the potassium especially since I've been feeling hyper lately, and pretty sure that I'm going to be going down to 25 mcg of hormone as soon as I get the results of my last blood test (if you remember, I started at 150 over a year ago). So I can vouch for the effectiveness of the supplements! Even more remarkable is that I'm hypo, and doctors tell us that it's impossible to get off the hormone!

One other note. Since I've been feeling so hyper, I've been experiencing the breathing difficulties again. I tried B-1 all alone, (200-400 mgs) and my breathing normalizes within 20 minutes. It's wonderful!

Thanks John, (oh yeah, in case you forgot, which is completely understandable, the main question here was about taking the potassium and magnesium together. I'm just excited!)

Penny

Subj: **potassium**
Date: 8/11/02 12:25:39 PM Pacific Daylight Time
From: btakacs1@yahoo.com
To: bu007@aol.com
Sent from the Internet ([Details](#))

Hi John,

I don't have thyroid problems but I came across your website while investigating isothiocyanates and goitrogens. I was interested in your information on potassium because many years ago I did a study in which potassium supplementation was used to eliminate symptoms of PMS.

I do not know if you know this but magnesium is the metal that is the coenzyme for the Na-K ATPase pump located on all cell membranes used to concentrate potassium inside of cells, where over 98% of the mineral is located. A magnesium deficiency in the presence of a potassium deficiency makes the potassium deficiency even worse. Replenishing just the magnesium will go some way into helping with the potassium deficiency because it will help concentrate it inside of the cell. Potassium supplements must be used to replenish a potassium deficiency because the acid-base balance that is usually messed up in a potassium deficiency must also be corrected in order for the body to retain the potassium. Using foods alone will not adequately correct a potassium deficiency. I never found any ratio that needed to be followed between the magnesium and potassium, just that both deficiencies needed to be corrected in the case of potassium deficiencies due to the role of magnesium in the Na-K ATPase pump. I did find however, that in order for the potassium to work on PMS (it took 3 months of daily potassium supplementation (600-1200 mgs/day) for the symptoms to go gradually away over this time) you could not touch phosphorous-free calcium or it was as if the potassium was not being replenished or working. Taking this form of calcium during this critical 3-month time would cause the complete return of symptoms and then you had to start the 3 month time period over. You could take dairy products, or any calcium naturally found in foods and this was fine. After the PMS is gone, taking phosphorus-free calcium was fine and symptoms did not return.

I did a hair analysis on myself throughout the time I was discovering this, about two years prior to the study I did, and it showed a very low potassium and a screeching high calcium. This was over 20 years ago but as I recall after correcting the potassium, my calcium values went down to normal. There is a study showing that use of calcium reduces PMS symptoms by 50%. Prior to discovering the potassium effects I had been on calcium and found this to be true. To me it was as if alot of PMS had to do with calcium balance, but that it could not occur in the presence of a potassium deficiency (whether due to the acid-base imbalance effecting the distribution of ionized/protein bound calcium or some other reason I do not know). Correcting the potassium deficiency corrected the calcium imbalance.

Anyways, thought you might be interested.

Sincerely,

Beckie Takacs

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Affect on Copper of Cortisol, Potassium, Disease

by Charles Weber

Copper nutrition is crucial for slipped discs, hemorrhoids, emphysema, aneurysms, and immunity.

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INTRODUCTION

I have previously proposed that rheumatoid arthritis is accentuated by losses of potassium in our food supply and is largely a chronic [potassium deficiency](#) [Weber 1974] which causes alterations inside the cell of free amino acids [Iacobellis], interference by sodium with enzymes inside the cell as a result of the increased sodium there [Rubini], alterations of the potassium- sodium regulating hormone patterns which then affect other physiological processes, or some combination of these.

I have come to believe that a disturbance of copper metabolism is the most serious symptom of these other processes. The aspect of copper physiology which is most potentially dangerous is its role in activating lysyl oxidase, the enzyme which cross links collagen and elastin connecting tissue.[Sandberg, et al]. Copper's effect on elastin is especially important because elastin gains its strength primarily from cross linking [Carnes1971(discusses copper aminases)] and because elastin is the main material of several important organs, which include blood vessels, spinal discs, lungs, and skin [Carnes, 1977].

Overall Copper Physiology

Copper, largely tied up as protein, enters the stomach, and there and in the upper intestine [Sachs, et al] [Underwood p70], the proteins other than those entering from the bile [Owen] are degraded (bile proteins are degraded in infant rats when cortisol is low [Mistillis & Mearrick]), thus making the bile the means of excretion for adults [Sarkar p246]. Loss in sweat is usually negligible [Underwood p74} as is losses in urine [Evans 1973b p547]. The copper is moved across cell walls possibly associated with certain amino acids [Neumann PZ & Silverberg M] [Sarka p236]. It may be alpha aminoisobutyric acid which is involved since this amino acid behaves the opposite of other amino acids from cortisol [Chambers, et al]. The copper moves past a metallothionein barrier inside the cells [Cohen, et al] into the serum. Both copper and zinc increase the metallothionein barrier [Oestreicher & Cousins]. The serum carries it largely complexed to albumin and histidine [Frieden 1980 p104]., to the liver. The liver rapidly [Peisach, et al p482] removes it and stores it until such time as unknown hormones (which probably don't include cortisol in any direct way) cause the liver to release ceruloplasmin (which protein contains copper) to the target cells [Frieden] for general purposes, as well as unbound copper when under stress. Adrenaline (epinephrine) stimulates ceruloplasmin release 150% [Weiner and Cousins] as well as free copper and may be the stress hormone for copper [Evans 1973b p556, 557] . I suspect the immune peptide hormones may be used for immunity but I have no data. The ceruloplasmin transporter is destroyed by the target cells which includes those which make bile proteins for copper excretion. Ceruloplasmin has a half life of 130 hours [Sternlieb]. The target cells could include the cells which synthesize tropoelastin (elastin precursor). If these cells synthesize Lysyl oxidase (which cross links connective tissue), they probably must incorporate the copper into the enzyme inside the cell [Harris, et al, p175].

In case of infection, decline of the effect of cortisol and corticosterone (not necessarily concentration itself) shut down unnecessary copper enzymes. Probably this is in order to provide increased copper to the immune system. In case of a potassium wasting intestinal disease, both DOC (deoxycorticosterone, a steroid hormone) and cortisol are used for this purpose. If these hormones shut down copper enzymes permanently by an ongoing potassium deficiency, I suspect health is degraded. The most serious effects are weakening of the elastin tissue derived arteries by inhibition of the lysyl oxidase system, along with fatty buildup in the arteries. Increased excretion in the presence of marginal copper intake can lower liver stores of copper sufficiently that the immune system can not operate effectively. These two effects, along with heart failure account for most of the mortality of rheumatoid arthritis. [Matsuoka].

ELASTIN CONNECTING TISSUE

Elastin makes up the vertebrate disks above the sacroiliac, the blood vessels, much of the skin, the lungs, and the bronchial tubes of all vertebrates except the jawless fishes [Sage & Gray]. The blood vessels are the most important because an organism can not remain alive after a large blood vessel bursts. Ruptured blood vessels are second after heart failure in deaths among arthritic people [Matsuoka]. Tough disks are fairly important also, because of their role in guarding the main nerve trunk. Lungs and bronchial tubes are not subject to such extreme stress. However, emphysema can be produced in animals by a copper deficiency [Soskel, et al]. The emphysema seems to have an

elastin defect greater than can be explained by cross linking alone [Soskel, et al]. and it is possible that an association will be uncovered in arthritic people, especially men, old women, or young women after a pregnancy. There is no current evidence that hemorrhoids are made worse by a copper deficiency, but limited experience leads me to believe that evidence will one day appear. I also suspect that a tendency to cut oneself while shaving will prove to be correlated also. If so, this would serve as a good early warning.

Numerous animal experiments have shown that a copper deficiency can cause diseases affected by elastin tissue strength [Harris].. Aneurysms of the aorta are the chief cause of death of deficient chickens. Men who die of aneurysms have a liver content which can be as little as 26% of normal [Tilson}. This researcher speaks of low copper as a marker of aneurysms probably to avoid embarrassment with his colleagues in ascribing it as causal. The median layer of the blood vessel (where the elastin is) is thinner but its elastin copper content is the same as normal men. The overall thickness is not different [Senapati, et al]. The body must therefore have some way of preventing elastin tissue from growing if there is not enough lysyl oxidase for it. Men are more susceptible to aneurysms than young women, probably because estrogen increases the efficiency of absorption. However, women can be affected by some of these problems after pregnancy, probably because women must give the liver of their babies large copper stores in order to survive the low milk copper.

Dilated superficial veins (varicose veins) are observed in copper deficient organisms*. Elastin is about as flexible as a rubber band and can stretch to two times its length [Carnes 1977]. Collagen is about 1000 times stiffer. A healthy artery requires about 1000 mm of mercury or 10 times the normal mean blood pressure in order to rupture [Shadwick].

COPPER ENZYMES

Other enzymes than lysyl oxidase require copper to activate them. One is undoubtedly a mechanism behind anemia. [Underwood]. Tyrosinase incorporates tyrosine into melanin pigment and is the reason why copper deficient sheep fail to pigment*. It is conceivable that human gray hair is also arrives this way. Low white blood cell count (neutropenia) is the earliest symptom in copper deficient babies [Cordano, et al]. The immune system is very sensitive to adequate copper [Prohaska & Lukaseqycz]. Copper deficient mice have lower number of antibody cells even though the spleen weight is greater [Prohaska & Lukasewicz]. The copper deficient spleens show little growth during an infection . The mechanism has not been elucidated. It is likely that several enzymes are involved, and white blood cells are rich in copper with four times as much as red cells [Mason p1993]. White cell count rises in affected babies within 2 or 3 days after supplement with 2 or 3 mg of copper per day and takes about a week to come to normal, which is a count of more than 1500 per ml for neutropenia and 5000 per ml for leukopenia [Holtzman, et al].

Supplements or copper rich foods should be used for babies with extreme care, as should be formula made from water out of copper plumbing (which can contribute 0.8 mg per day to adult intake [Delves HT]), or brass pots (which have harmed American Indian children [Bremner p45]), because babies can not excrete copper. Nursing babies would be even a little more at risk from supplements since mother's milk contains five times cow's milk [Delves p7]. Babies have 19 mg total copper at term, half in the liver [Klevay 1996 p2424]. New borns have 230 ppm (parts per million) in the liver which compares to 35 ppm in an adult It must be obvious that 3 mg per day would overwhelm a baby in a short time if continued. Mason says that infants should get 0.05 mg/Kg per day and premature infants should get 0.09 mg/100 Kcal [Mason p1998]. I do not know at what age they can excrete copper. However they are said to have a an adult like liver in two years [Evans 1973b] and their serum levels increase to near adult levels in one month (4-6 months for preterm) [Lonnerdal].

Several brain neurotransmitters such as dopamine and norepinephrine are formed by copper enzymes. The brain other than the cerebellum and hypothalamus have these transmitters decreased 30% to 60% in various sectors by a copper deficiency [Feller 1983]. It is possible that this is part of the poor muscle tone and motor response sometimes observed in a deficiency*. Perhaps copper should be investigated for Parkinson's disease. Copper is thought to increase perception of red and green color [Isaacs, et al].

It has been proposed that copper deficient embryos cause increased genetic defects [Jankowski, et al]. The authors suggest that the problem may arise because of oxidative damage to DNA produced by reduced superoxide dismutase (SOD) which is an enzyme which degrades superoxides. Velo, et al have proposed that control of free radicals by ceruloplasmin, but actually presumably by SOD, is the protective role of copper against inflammation [Velo, et al]. More likely any role of copper deficiency in inflammation probably operates through the prostaglandin hormone system (possibly PG-f2) [Sorenson p252] [May & Williams p296].

Diabetes

Copper depletion doubled glucose in blood of diabetic rats fed glucose, 50% higher for sucrose [Cohen, et al 1982]. There must be a copper catalyzed enzyme somewhere in the process, therefore. One investigator has suggested that buildup of copper in the kidneys of diabetics is responsible for the kidney damage which sometimes appears in diabetics (based on rats) [Failla & Kiser]. Diabetics probably absorb copper two times more readily than normals [Craft & Failla]. Diabetics may have a narrow safe range of intake. The pancreas can be irreversibly destroyed by a copper deficiency in rats inside a few months, but the isles of Langerhan are not affected [Smith, et al] [Fell]

Recurrent diarrhea is often observed in a copper deficit [Underwood]. This may be related to the known sensitivity of the immune system to copper. Copper deficient rats survive one third as long as normal which have been infected

with Salmonella typhimureum [Newberne & Gebhardt]. Scurvy like bone changes are a long term result [Underwood], probably caused by failure of bone collagen to cross link [Siegel & Martin (they named lysyl oxidase)]. It is very unlikely that this can be corrected by future intake because of low bone turnover, so adequate intake is crucial for older babies. Osteoporic bone with bone ends in children (similar to scurvy) should cause the first thought to be a copper deficiency [Delves p19]. The age at which human babies stop degrading bile copper protein is unknown to me, although it probably happens gradually. Collagen does turnover, but very slowly. Bone collagen is so slow that correct intake in childhood is essential. Elastin probably has a high turnover [Robert] and also may be porous to the enzyme. I feel that improvement in less than a week is reasonable to expect for elastin tissue {Author's experience}. This is fortunate in view of the extreme danger from elastin ruptures.

A copper deficiency has the characteristic of increasing cholesterol in the blood stream [Allen & Klevay]. A histidine induced cholesterol rise is abolished by copper supplements [Harvey, et al]. It has been suggested that a high zinc to copper intake ratio is an important part of this [Klevay 1978]. The rise in cholesterol and triglycerides has been attributed to a 40% or more reduction in lipoprotein lipase. I do not know whether this is a copper enzyme or not. This may be an adaptation to provide extra cholesterol for lining the arteries with deposits in order to help protect them against rupture by decreasing their internal diameter for the stress on the walls is directly proportional to the radius. Whatever the evolutionary stimulus, copper deficiency is a much more plausible explanation of high serum cholesterol than any difference in cholesterol intake, since the body can synthesize its own cholesterol and average cholesterol intake has not varied more than 5% in the last 100 years*. No enzyme system has been linked to this phenomenon yet with certainty to my knowledge. However the reduction of lipoprotein lipase during copper deficiency has been proposed [Lau & Klevay]. Non ceruloplasmin copper is said to signal the increase of cholesterol [Harvey, et al].

Cholesterol lowering drugs

have not prevented deaths. and the cholesterol level is normal in the average heart attack victim

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Potassium Deficiency

Some of these symptoms also appear in arthritic people. I believe I now see how potassium deficiency may be disturbing metabolism in order to produce them. Potassium wasting infectious disease is the most likely reason for a severe potassium deficiency in nature, not nutritional failure. I propose that the body uses the electrolyte hormone system to stimulate part of the immune system and to alter the basic physiology in order to mobilize the body's defenses against a lethal intestinal disease. Infections of the intestinal tract should be difficult to detect, and the diarrheas, including cholera, may be examples of the type of potassium wasting diseases which forced this system to evolve. Even in the modern world diarrhea is a major cause of death in children, especially in the tropics.

Resisting infection is an extremely important function of the body. It is even related to predation because a diseased animal has great difficulty escaping. It is therefore plausible, as I am about to propose, that numerous physiological processes are fundamentally altered in order to more effectively fight off infection, in the above case, diarrhea [Weber 1998]. The immune system is considerably weakened by inadequate copper as mentioned above. It is therefore logical for the body to attempt to increase the copper available to the white blood cells during disease. It would also be desirable to signal this increase using a hormone system which does it by declining effect. Otherwise a pathogen could evolve which could consistently overwhelm the immune system simply by making an enzyme which destroyed the hormones. Shutting down enzyme systems which were not immediately essential to immunity is one way to increase availability of copper.

11 Deoxycorticosterone (DOC) is a hormone probably used by the body to regulate sodium and potassium when intake of both of them is high. It declines during a deficiency of potassium and sodium. [Weber] It stimulates collagen synthesis [Popisilova] and would thus tend to cancel cortisol's [[Houck & Gladner] effect during diarrhea. Thus the collagen effect would not obtain during diarrhea when serum amino acids are of little consequence and collagen would not be compromised. Any compromises during diarrhea would not be important compared to the urgency of defeating or mitigating virulent diarrhea. However if there is an inappropriate potassium deficiency coupled with the high cortisol of emotional stress which goes on for years, connecting tissue may be weakened. The DOC effect is probably accentuated by low sodium.

The effects of muted cross linking by cortisol drop are especially serious for elastin tissue because the disordered rubbery organization of elastin depends entirely on the cross linking for strength [Sandberg, et al]. Lysyl oxidase oxidizes the amino group in lysine [Siegel & Martin] which amino acid is common in elastin. The aldehyde which forms spontaneously combines with adjacent amine and aldehyde groups to form strong covalent bonds and thus join together the fairly small protein precursor molecules. The same thing happens for collagen and bone also [Siegel & Martin], but collagen in tendons has many less cross links [Kelly & Harris, p227], probably made possible by collagen's greater length and more ordered structure which permits numerous weak hydrogen bonds to be effective. The strength of pig or chick tendon is little affected by copper deficiency, even though the animals are dying of ruptured aortas and even though the tendons have 70% the cross links of normal [O'Dell] [Chou]. The normal lesser number of cross links are desirable, for they permit the tendons to return to their original position after stress is relieved and not to cold flow as polymers held together only by hydrogen bonds do. The number of cross links are probably optimum, because too many would make the tendon brittle. Too few cross links would cause the tendon to become slack with time. Thus the body has a tough material which approaches steel in strength weight for weight and bones which are almost as strong as cast iron (I do not know how cross linked bone collagen is although both bone and tendon are type I collagen [O'Dell]). The lesser reliance by tendon collagen on cross linking for

strength may be the reason why the body uses collagen to repair lesions in arteries during a deficiency instead of elastin [Waisman, et al]. Such a strategy may be a good immediate expedient for survival, but I suspect it results in an intractable hypertension eventually because collagen is less rubbery or elastic than elastin.

Superoxide

It has been proposed that the immune system generates superoxide in order to help kill bacteria*. Normally the copper catalyzed [Fridovich] superoxide dismutase enzyme destroys superoxide radicals, which are derived from white blood cells (neutrophils, eosinophils, and macrophages) [Smith & Bryant], as fast as the radicals form. This enzyme declines during infection [Flohe, et al] and is undoubtedly used by the body to help defeat serum infections [Smith] [Ghosh & Chatterjee]. Thus there would be a double advantage in diverting copper from this enzyme. I do not know yet whether decline of this enzyme is tied to the potassium hormone system or not. Superoxide degrades the joint fluids by de polymerizing hyaluronic acid [McCord] and possibly collagen [Sorenson 1978 p252] as well as bacteria. I suspect that this is an unavoidable compromise, tolerated because of the extreme urgency of fighting disease. Decline of superoxide dismutase has been proposed as one of the mechanisms accounting for some of the symptoms of rheumatoid arthritis [Sorenson 1978], which is an indication that this enzyme is indeed tied to the potassium enzyme systems. Superoxide dismutase is low in children with rheumatoid arthritis. Injections are said to be beneficial in osteoarthritis [Rister, et al]

Glucocorticoids

I propose that the primary purpose of glucocorticoids (steroids oxygenated in the 17 carbon position) is to mobilize the body to resist infection. They do so by normally altering processes which increase pathogens' growth or adverse effects and then declining when under attack. As already mentioned this inverse style is much safer for resisting infection. I propose that cortisol is for intestinal disease and corticosterone for serum disease. Glucocorticoid mobilization for fight or flight is an adjunct made possible because most processes which resist infection are an antithesis for fight or flight [Weber 1998]. Release of ceruloplasmin copper transport protein from the liver is useful for both situations and is therefore controlled by a different hormone, epinephrine, for fight or flight [Evans 1973b p556, 557].

Potassium loss is the most serious aspect of intestinal diseases, so the electrolyte capabilities of cortisol, but not corticosterone, are oriented around conserving potassium by migration into the cells upon decline of cortisol [Knight, et al]. Cortisol, but not corticosterone, has its secretion from the adrenal cortex markedly reduced by low serum potassium (in vitro, that is test tube, experiments) [Mikosha, et al]. Sodium, water, glucose, amino acids, chloride, hydrogen ion, white blood cell activity, copper enzymes, and numerous other hormones and enzymes are controlled by [cortisol](#) such as to survive during virulent intestinal disease [Weber 1998]

Cortisol works by declining effect, not necessarily declining concentration. Indeed, in most diseases glucocorticoids actually rise. However, at the same time T white blood cells secrete a protein, glucocorticosteroid- response modifying factor (GRMF), and the protein hormone interleukin-1 both of which inhibit the effect of cortisol on white blood cells other than the suppresser cells [Fairchild, et al]. The effect of GRMF on physiological processes is unknown at present. The husband and wife team working on GRMF were almost murdered and this disrupted current investigations. I suspect that most of cortisol's effects on copper enzymes will prove to be involved with GRMFs. These two protein factors thus raise the effective set point of cortisol. This system also uses interleukin-1 to stimulate the production of ACTH, and thereby also cortisol, instead of the brain's corticosteroid releasing factor (CRF) which last is used in the absence of infection. The immune cells thus take over their own regulation.

Cortisol

Cortisol, like DOC, also stimulates lysyl oxidase activity [Siegel], and undoubtedly for the same reason, that is to provide extra copper to white blood cells during infection upon decline. Its action on collagen is exactly the opposite of DOC's: [Popsilova & Popisil] for cortisol inhibits collagen formation [Manchester p273]. This is significant because collagen is the most bulk of protein, is inert, and makes relatively non vital structures, the skin being especially targeted by cortisol by ten times [Houck, et al][. This attribute of cortisol would be a desirable attribute if the pathogen were in the serum, because increased synthesis of collagen when cortisol declined would considerably lower free amino acids in the blood stream, and thus slow down bacterial growth. There would be little advantage from this during diarrhea, and this may be why DOC acts in the opposite direction and thus counteracts cortisol's effect when diarrhea is involved.

I submit that potassium would be a lot safer way of increasing cortisol than use of injections. Steroids are hormones, not pharmaceuticals. Their sole purpose is to keep important body functions and concentrations at values optimum for survival. There should be no reason why artificial additions should be necessary under normal conditions and adequate nutrition for anyone free of genetic defects (which is undoubtedly almost everyone). Quite often a steroid is injected with impunity and seemingly no immediate obvious adverse symptoms. But this is usually because other hormones alter in an attempt to adjust the imbalance and because many of the adverse symptoms such as, for instance, negative feedback which causes reduction in secretory cells of the hormone is a long time in materializing. One medical writer summed it up so: "it is remarkable how effective cortisol is in getting a seemingly hopeless patient on his feet again. Sometimes it is so effective, he can walk all the way to the autopsy table".

CERULOPLASMIN

Ceruloplasmin is higher than normal in the blood serum of arthritic people [Aiginger, et al]. The total serum copper concentrations are bimodal for the distribution of these people with the bottom mode about the same as normal people or people with osteoarthritis [Youssef, et al]. It could be that the bottom mode was from misdiagnoses.

Ceruloplasmin is almost certainly used as a transport protein to bring copper from the liver to the target cells [Frieden] in addition to its other transport uses. Ceruloplasmin is a blood protein which contains 6 [Frieden] or 8 [Sekiya, et al] atoms of copper inside the molecule which are not in equilibrium with the serum [Pelsach, et al]. Such a transport mechanism would be extremely useful in case of infection, because, since ceruloplasmin's copper is not in equilibrium with the serum, it is thus not available to pathogens. With that many copper atoms it is conceivable that it can give up its copper in more than one way. It must be destroyed in order to give up all its copper. Ceruloplasmin's half life is 130 hours [Sekiya] but has a higher turnover in rheumatoid arthritis [Sorenson, 1978 p217]. One of its copper atoms may be exchangeable under reducing (anaerobic) conditions [Peisach], however. The hormone which causes rise of serum copper and ceruloplasmin from the liver because of stress may be epinephrine (adrenaline) [Evans 1973b p556] [Meyer, et al]. Cortisol is not directly part of it, although decline of ACTH which regulates cortisol may be for immunity [Evans 1973b p554]. Cortisol does stimulate the formation of metallothionein four or five fold, the copper storage protein [Piletz & Herschman]. Thus copper should become more available for ceruloplasmin synthesis inside the liver upon decline of cortisol. The main advantage of this last may be to help drain the intestinal contents of copper to deny copper to diarrhea bacteria, however. It may be cortisol decline which inhibits bile flow after adrenalectomy (amputation of adrenal glands) to conceivably further that same denial [Evans 1973b p556]. DOC decline inhibits liver copper uptake and increases free copper secretion from the liver [Grogriadis & Sourkes]. This is logical since the serum copper can not nourish diarrhea bacteria.

The mortality of chicks from salmonella infections rises significantly from zero if large amounts of copper as copper sulfate is fed, which supports the contention that this is the reason why their bodies increase ceruloplasmin four fold or even as much as six fold [Underwood p58] during infection but not equilibrium copper bound to albumin and histidine [Starcher & Hill]. This concept is reinforced by the fact that chicks in the absence of infection have a very low ceruloplasmin serum content [Starcher & Hill] unlike mammals. The fact that people with Wilson's disease are not susceptible to infection even though they cannot synthesize ceruloplasmin does not refute ceruloplasmin's role proposed above. This is because people with Wilson's disease can not excrete copper so that their cells are already loaded and even overloaded with copper. The high ceruloplasmin content of mammals in the absence of infection may originally have been an adaptation from their immune use to supply extra copper to the embryo by females. Even today human females have a higher ceruloplasmin content than males do [Frieden 1980 p110]. There may be a similar advantage keeping free copper from fungi as well as bacteria if a limited experiment I tried is an indication. Bacteria could not make use of the copper in ceruloplasmin unless they were to evolve an elaborate mechanism for preferentially binding the ceruloplasmin and then degrading it. This would be an unlikely occurrence. Ceruloplasmin declines in the serum greatly during a deficiency [Gomi]. This would not itself affect immunity except the ability to increase ceruloplasmin during infection is probably decreased also.

Something about ceruloplasmin may be related to Parkinson's disease [Frieden 1980, p108].

It is possible then, that the best way to relieve a copper deficiency which is concurrent with a bacterial infection would be by ceruloplasmin injections. Such a procedure would bear investigation since it is unlikely that people will change their diets and eat enough copper or delete copper physiology poisons which may include tobacco. White blood cell count is very sensitive to copper status and is the earliest and most consistent symptom of a deficiency [Cordano, et al]. Even a mild deficiency causes spleen derived immune cells to be significantly less competent as stimulators in general and also to be stimulated by endotoxin, pokeweed, and concavalin A [Lukasewicz & Prohaska]. Such animals took an average of one third as long a time to die as replete animals, and had four times the mortality [Newberne & Gebhardt]. I believe that the efficacy of adequate copper prior to an infection is established beyond any reasonable doubt. Dietary copper during an infection may be disadvantageous however, except during a deficiency, when it probably would be best to spread it out across the day complexed to protein. A depleted liver removes free copper from the blood with extreme rapidity, [Peisach, et al] however, so the danger is probably not acute.

Since ceruloplasmin is probably used to transport copper to the bile for excretion, excretion may inadvertently rise when ceruloplasmin rises during infection (I have no data to establish this). A similar mechanism may account for the higher ceruloplasmin content in the serum of arthritic people. Apparently decline of cortisol is not used for this purpose and the hormones which do are not known for sure. There could therefore be an increased excretion arising from the higher serum content of arthritic people. If this is so, arthritic people may need somewhat more copper than others until their potassium deficiency is relieved. This may be why their liver copper is low, why their whole blood copper does not rise even though the serum is high [Sorenson 1978, p217] and part of the reason why they are much more likely to die from ruptured blood vessels (aneurysm) and infection than others [Matsuoka, et al]. Thus rheumatoid arthritis could be viewed as often a multiple deficiency, not all of the symptoms of which can be always removed by supplying only one of the missing nutrients.

Arthritic people also have a higher free copper content in their blood serum [May & Williams p294]. This would seem at first glance to be at variance with the concept that arthritis is an inappropriate immune response. However, intestinal diseases should not be affected much by free copper in the serum, so that immune copper responses accentuated by potassium deficiency may have some subtle differences from responses which are involved primarily with serum infections. Free copper may be more useful to an animal when muscle exertion is needed, because when sheep which have been subjected to a copper toxicity hear the bark of a dog, so much free copper can suddenly be released from the liver that it can kill them [Bremner p42]. Therefore this may be additional indication

that people who have a serum infection should be guarded from fear. Free serum copper may be useful to someone with intestinal disease so that he can operate optimally. In addition, the vigor of copper's absorption may even be increased in babies in a diarrhea situation because of the decline in cortisol mentioned previously. Thus diarrhea bacteria would have the use of less copper. I have no assurance that this is the case in adults, and indeed corticosterone injections cause greater secretion of bile in baby rats but not in adults [Evans p234]. This may be an adjunct of corticosterone, used to get baby rats out of the non excretion mode. Rats are a poor experimental animal for this concept because they do not secrete cortisol. They probably were able to lose that secretion because they have a marked inhibition of cholera toxin by something in their intestinal fluid [Donowitz & Binder] and because their ascending colon absorbs water under c-AMP stimulation unlike their descending colon and other mammals [Hornick, et al]. Rats should not be used for any experiments involving immunity, and perhaps better yet, for none.

Copper in the Diet

A copper deficiency is possible even without the inappropriate requirements of a potassium deficiency proposed. Processing food often lowers copper content. The standard hospital diet is less than 0.75 mg per day [Owen p13]. None of 40 ready to eat cereals had copper or manganese although 50% and 25% or more respectively for the MDR of iron and zinc was supplemented. 25% of supplements contained no copper [Johnson]. Zinc without copper is very dangerous. Diets of free choice are 1 mg per day [Holden, et al]. Western diets usually range between 2 and 4 mg per day and 20 USDA diets contained 1.05 per day [Mason p1998]. This compares to 4.5-5.8 mg per day in the Indies [Peisach p1998]. Intravenous is suggested to be one third the oral intake [Mason p2036]. The unpopularity of the rich source, liver, and the high cost of shellfish reinforce this situation for poor people not in the military (the military provides occasional shellfish). 2 mg per day is thought to be the minimum daily requirement (MDR) [Klevay 1982] and I suspect that 4 mg per day would be the safest intake (RDR) in order to cover everyone or perhaps the 6 mg. received in the Indies.

Lending some support to this contention is the circumstance that underground Utah copper miners had 15.1 accidents per 200,000 man hours with no lost time Vs 10.9 accidents with lost time to give a ratio of 1.4. The figures for all underground Utah non copper miners were 4.4 and 8.4, giving a ratio of 0.5 [US Dept. Labor] as computed from bureau of mines statistics. There are figures for Arizona [Inzan & Hoyle]. Figures from other states trend in the same direction for underground mines, open pit mines, and processing plants. This would seem to indicate that copper miners are tougher than other miners, since each injury is less likely to cause lost time for copper miners. Also, the greater number of injuries to copper miners suggests that their greater toughness tends to make them more careless. The figures might have been even further apart if injuries not connected to strength such as eye injuries and burns had been removed from the data. New Jersey copper smelter workers have 8% of injuries as back injuries vs. 20% for all other occupations. Two hundred and eighty patients having severe back pains were treated with copper salicylate. A majority were believed to have a slipped disc. Improvements were considerable and rapid [Sorrenson & Hangarter]. Finnish copper miners are said to have much less arthritis and the women miners less anemia than other Finns [Sorrenson p223]. Finns have a lower copper intake than Americans, and as little as one half the intake of Africans and Asians, [Mason p1083] probably partly because of a high milk intake. Finns have the highest arthritis rate in the world, [Kellgren JH] possibly partly because of perspiration losses during saunas. Such figures suggest an environmental cause rather than genetic, and probably not climatic because Laplanders not much further north have a lower rate, while Masai people [Best & Taylor p768] join the Finns' low rate probably because of their milk intake also as well as low vegetation in the diet. Males who die from aneurysms have one fourth the tissue copper and two thirds the liver copper contents upon autopsy than normal [Tilson]. Since young women are not as affected by copper deficiency as men generally it must be because estrogen enhances absorption [Cohen, et al]. I suspect that this is an adaptation to furnish babies with sufficient copper to surmount the low intake while nursing milk. This is evidence that disruption of copper in arthritis is secondary because women have arthritis much more often than men.

A pervasive copper deficiency would be suggested from the beneficial effects of copper supplements on such diverse diseases as anemia, psoriasis, ulcers, ankylosing spondylitis (Ankylosing spondylitis probably heals slowly because the sacral and ileal joints are made of type I cartilage [Paquin, et al]. The lower ceruloplasmin in that disease may also be implicated in some way) [Sorrenson 1978, p223, 225, 253], infection, cancer [Nriagu], impaired growth of the retina [Danks p211], seizures as discussed by Sorrenson, and deficiency creates atherosclerosis of the kidneys [Owen] since some of these diseases are common in our society. Copper supplement has healed slipped discs (in combination with pharmaceuticals). A copper deficiency may be the cause of arrhythmias associated with use of liquid protein diets [Klevay & Viestenz] (this reference has EKG data). If these diseases are related to copper there should be a correlation between them, but I have no information for this. Copper helps in removing abnormal EKGs caused by copper deficit but is not always on time, and did not prolong life indefinitely [Viestenz & Klevay]. In addition, any problem which is a function of strength of elastin tissue has a high probability of being accentuated by a copper deficiency. Several of these symptoms together would make the probability of a copper deficiency existing very high indeed and anything which would reduce or interfere with copper very dangerous.

If I am correct in this, there should be very little of these strength of elastin tissue diseases among people who eat a lot of shellfish, especially east coast oysters [Mason p1998]. Some of the advantage of east coast oysters may have disappeared now that the copper smelters have moved west to be near the mines. Shellfish use a copper pigment instead of iron to transport oxygen.

Squid and sour bugs are included for this circumstance. Squid has a fairly large fraction of the copper in the skin. It may be that they use the skin for excretion because the skin also contains much of the cadmium [Gajewska]. Cadmium causes changes similar to a copper deficiency [Lefevre, et al] [Festa, et al]. Copper tends to mute the toxic effects of cadmium [Costanzo, et al] and silver [Underwood p72]. Even so, it is probably best not to use the

skin of squid.

The richest source of all is sheep liver, about two times cow liver and duck liver, and about ten times all other livers*. These other livers range from about 7 to 14 mg per pound. Dog and cat foods are also high in copper because copper is added. I do not know what the averages are for them. However, they are probably at the very least a fair source for poor people.

Vegetables high in starch have about 1 mg per pound. Legumes have a range the same as most livers, as do some oil seeds. Cereal grains are about half this. However do not be misled by figures based on weight for food which contains no water. Foods containing water have to be multiplied by the inverse of the water content to be comparable, or better yet, compared on a calorie content basis.. A dried apricot has exactly the same mineral content as it had directly from the field, for instance, per calorie or per weight. Leafy vegetables are probably higher than starchy vegetables, but I have no figures at present. Honey is very low, comparable to milk. [Lawler & Klevay]

Drinking water can contribute as much as 0.8 mg per day if it comes through copper pipes. Soft water and acid water contribute the largest amount [Sparrow, et al]. Copper bracelets are a rather ineffective source, but can have a small measurable effect on arthritis, especially in summer.[Walker & Keats]. It probably would be significant if a dozen or so wide bracelets were worn in summer, especially if they were corroded. I suppose for people who refuse to gain copper any other way it would be better than no way. I suspect that there will prove to be a strong negative correlation between acid water from copper pipes and aneurysms, slipped discs or hemorrhoids.

Milk

The poorest unprocessed source is milk. It contains less than 1/4 mg per pound. This may be an adaptation to protect the mammary glands or the baby against microorganism growth. Babies solve their copper problem with large stores in their liver. Adults who eat large amounts of milk would be at more risk if they had no other good source of copper. Milk is the food scientists use when they wish to create a copper deficiency in animals. This low copper content may be part of the large increase in cardiovascular disease which has been statistically associated with milk. [Seely] [Klevay 1974]. Milk is said to be a greater risk factor than smoking cigarettes. All the cheeses are included in this category. If its copper content is the cause of its being a risk factor, correcting the problem should prove to be very easy.

The necessity of dealing with this circumstance is no doubt the reason for the different handling of copper by women vs. men and the strong effect of female hormones on copper physiology. The lesser effects of copper supplements on women with arthritis*, the much less rate of aneurysms among women, and the tendency for these differences to recede as women get older is probably related to that necessity. What little copper is in milk must be part of its cellular components. Copper must be virtually unavailable to most bacteria attempting to live in milk, and this may be the reason why women evolved the ability to give their babies copper through liver storage rather than by milk content.

Interfering Food Elements

Eating large amounts of zinc interferes with absorption of copper [Fischer, et al] [[Cheek, et al]. Using "all purpose" vitamin supplements devoid of copper such as used to be prevalent is thus rather dangerous. Eating large amounts of vitamin C (ascorbic acid) is thought to interfere with utilization of copper within the body [Underwood p71] although Evans thinks absorption is decreased [Evans 1973b]. Vitamin C causes ruptures of the aorta in deficient animals [Owen]. I do not know what the mechanisms are. Gaining carbohydrate in the form of sucrose or fructose will more than triple the mortality from ruptures in the top of the heart in copper deficient rats [Reiser]. So far as I know the mechanism is unknown. Phytates which are found in wheat tend to decrease absorption somewhat [Underwood p71]. A copper metabolism poison has been found in one of the wild nightshade plants Childers & Russo, so that it is conceivable that the tame nightshades, tomatoes, potatoes, egg plants, peppers, and tobacco have vestiges of something similar. Sulfide acts to inhibit absorption [Sarkar] p238], which might be of interest to those who still take sulfur and molasses. Molybdenum causes symptoms of a copper deficiency even though the liver copper stays high [Evans 1973b]. The minimum daily requirement must then be partly a function of the status of one's other nutrition. I feel that it should be possible to receive enough copper even if all the above interferences are present, although I know of no research which establishes this. Someone who is receiving marginal amounts of copper, however, appears to me to be in grave danger if even a few of the above interferences are present. It may be prudent to cut back on most if not all of them.

Copper Toxicity

Too much copper is toxic. The amounts showing acute toxicity are large. A man sized pig must receive over 200 mg one time to show obvious acute signs [Higgins]. About ten times this amount is a favorite way to commit suicide in Bombay, India*. I suspect that a chronic toxicity for years can cause loss of weight, high blood pressure (salt intolerant), impotence, loss of ability to excrete potassium resulting in nighttime muscle spasms, and lymph edema. I suspect that most of these symptoms probably arise from a concurrent zinc deficiency because of interference with zinc absorption. The edema could conceivably be connected with disruption of potassium channels. In a study, Choe and his colleagues used X-ray crystallography to resolve the structures of four potassium channels from the sea slug *Aplysia*. The channels, called Shaw, Shab, Shal and Shaker, represent the four classes of potassium channels found in all higher organisms, including humans. With the exception of Shaker, all of the channels contained four zinc atoms in analogous positions. "Each channel resembles a funnel," said Choe, "and the zinc elements ring the end that empties into the cell's interior." Neuroscientists have known for decades that dyes that bind to zinc stain brain

cells in unique patterns, indicating that zinc should have a role in brain function. And studies have shown that zinc can enhance learning in undernourished children. The nature of zinc's organization in the brain, however, had been unclear.

Copper does not interfere with zinc as badly as zinc interferes with copper [Cheek, et al] but it does interfere. I suspect that swelling of prostate tissue via a zinc deficiency accounts for some of the above symptoms by interfering with bladder emptying.. A zinc deficiency may be connected to swollen prostate tissue, since zinc inhibits prostate growth*.

Toxicity

Some members of society are or may be at great risk from copper toxicity. People who have Wilson's disease (a genetic inability to synthesize ceruloplasmin), one of the three most common forms of schizophrenia*. and babies head the list. For some reason schizophrenia and rheumatoid arthritis seldom occur in the same person while a group of ankylosing spondylitis patients almost all had schizophrenia or an atypical psychosis [Osterberg 1978]. Diabetics are more efficient at absorbing copper, and may have a narrow safe range as already mentioned. For a discussion of copper toxicity see <http://www.merck.com/pubs/mmmanual/section1/chapter4/4j.htm> .

Two mg per day has been recommended for copper deficient babies, but I suspect this is much too high if maintained. Premature babies are usually born with too small a liver reserve to get safely past the nursing period, but one must use care with supplements. 0.09 mg per 100 Kcal has been recommended [Mason p2028]. I suspect that a seat of the pants criteria for such babies would be little more totally than the amount in the liver of normal babies above and beyond the amount they otherwise would receive in their milk. Normal should probably be two or three times as much per body weight as adults require or about 0.08 mg/Kg. and 0.04 for toddlers Perhaps that ratio should be less for very fat babies. A full term baby has 230 parts per million of copper in its liver*, or 105 mg per pound of liver. I know of no way to determine clinically how much it actually contains although modern ultra sound devices should be able to determine liver size. Red blood cell superoxide dismutase has been proposed as a good criteria of copper status in rats

[Feller, et al]. Serum contents are not a reliable indicator since infections, emotional stress, and possibly potassium deficiency have an overriding effect. Liver biopsies are impractical but would be the best way if they were available [Klevay & Madeiros, 196, p2423S]. Hair analysis is ambiguous, does not change much [Danks p222], and subject to contamination. Marginal copper deficits do not change serum copper, or tissue copper-zinc superoxide dismutase enzyme even though ultra structural alterations in the heart, reduced copper in the brain, markedly decreased IL-2 production, and reduced immune function appear [Hopkins & Failla].

Copper combined with a wide range of chelating agents have been recommended for rheumatoid arthritis [Sorenson & Hangarter]. I have no evidence that such a strategy is unusually dangerous. However, I think some caution is in order because when lysyl oxidase activity increases, blood pressure does also [Iwatsuki et al]. It is not possible that inhibition of this enzyme operates through artery wall thickness because the effect takes place in a week. I suspect that this is an adaptation to help protect arteries weakened by copper deprivation from rupturing. If massive doses are given it is conceivable that this protection could be defeated before arteries have a chance to strengthen. Elastin has a fairly high turnover rate [Robert] and lysyl oxidase has a half life of only 16 hours [Siegel]. However strengthening is hardly instantaneous. I suspect one must allow at least a week for sure significant strengthening. A normal body contains only 150 mg of copper*, so even someone containing only half of normal should be able to correct a deficiency in a reasonable time with a total intake no more than ten mg per day (8 mg supplement), but cutting intake back to 6 mg total or so total [Osterberg 1980 pp. 135, 142] upon repletion and making sure that seven times as much zinc is taken with the supplement dose. Completely safe

supplementation for people with weakened elastin tissue may yet prove to be a little less than this or should be this but coupled with blood pressure medicines. In animal experiments adequate intake may be 5 to 10 times as high as intakes which cause deficiencies [Klevay & Madeiros 1996 p2422S]

It is possible that growth of fungi is enhanced by free copper. Growth is enhanced by externally applied copper. That large amounts of copper can be toxic should definitely not make one reluctant to use reasonable copper supplements if you are not in one of the copper abnormal groups mentioned above. For normal people on a marginal diet I suspect that a supplement of 4

mg per day would be adequate and very desirable. I suspect that amounts 2 or 3 times this would have little adverse affect, but I know of no experiments. People eating unprocessed food devoid of milk and in an active life probably usually need no supplements or extra liver. However if you have a slow healing spinal disk, varicose veins, shaving cuts, hemorrhoids, or emphysema I would warmly recommend at the very least considering eating shellfish. Elastin diseases are extremely dangerous.

Effect on Society

The degenerative diseases mentioned above (aneurysms, slipped disc, hemorrhoids, emphysema, arthritis) are among the most destructive, painful, and numerous in our society. If copper status is an important parameter affecting them as I suspect, increasing copper intake should have a dramatic effect on our collective health. That copper is below optimum in a large number of people is virtually certain from current evidence. People vary considerably in their genetic makeup, and there are several dozen enzymes and hormones containing or affecting copper, so it should not be surprising that the symptoms of rheumatoid arthritis and the other diseases above should vary greatly or that "spontaneous" remissions are possible. When you further consider that other nutrients

and circumstances also vary enormously, especially for those eating processed food, it is not safe to assume that copper is not deficient because all the symptoms are not present. Any symptom should trigger consideration of increased intake from some source.

Clinical Strategies

It seems to me that injections of GRMF and interleukin-1 along with other hormones secreted by T-cells would be of considerable value in fighting AIDS if done right. Small amounts injected every ten minutes or so would be the only efficacious way since the half life of the protein peptide hormones is usually low, as little as 6 minutes in the case of cachectin. [Hall & Goldstein]. If T-cells prove to be responsible for mobilizing copper but the hormone can not be isolated, I would suspect that ceruloplasmin should be injected also but its long half life would seem to make unnecessary frequent injections. If secretion of immune hormones responsible for removing cancer in the body such as the synergism which has been demonstrated between interferon and cachectin (tumor necrosis factor) for breast cancer* prove to be dependent on copper for maximum production, ceruloplasmin injections may be in order for people who refuse to eat copper in addition to injections of those hormones. If injections of these peptide hormones are the only way to resolve the situation many small injections are the way it should be done. Massive injections once a day such as are currently used are both ineffective and dangerous. Frequent injections may seem irritating to the patient and unprofitable to the medical profession, but the main consideration is to get rid of the disease. When the hormone massively injected is insulin, wild swings in other hormones are also created, notably 18 hydroxy deoxycorticosterone (the potassium retaining hormone) and probably cortisol also. It is possible that diabetics subjected to such drastic swings have the disadvantages of some of the worst effects of both the high and low states, especially in the case of cortisol. It may be the source of some of the health problems that diabetics are afflicted with.

I would also suspect that if strains of bacterial diarrheas could be developed genetically devoid of their ability to synthesize the c-AMP stimulating enterotoxin and encapsulated in an enteric tablet in overwhelming numbers in order to avoid destruction by stomach acids, it might be possible to prevent most of the potassium loss implied in those diseases by competition of the mutant strain with wild cholera and thus not be hung solely on the cortisol system to survive. It might also prove to prevent the disease during an epidemic. When the patient goes back to eating food again, it might be a good idea to start with foods low in copper such as milk and honey, and of course oral rehydration (ORT) salts right from the start, which include potassium, which last is now done. If copper is low ceruloplasmin injections would probably solve the problem of using low copper foods.

There is no excuse for humans to have a copper deficiency. Shellfish are excellent sources and have already been part of successful farming procedures (oysters) or have a high probability of being able to be farmed without too much environmental damage (shrimp). In addition there are vast tonnages in Antarctic krill. Furthermore some species of terrestrial snails are considered pests and actually exterminated and discarded. For those who have religious or quasi-religious convictions, or taste instincts against eating shellfish or liver, supplements are inexpensive. There is enough copper in one small electric motor to keep a whole town supplied for quite a while. Better the copper into supplements than into a motorized wheel chair, but always in moderation and with seven times as much zinc.

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PROLACTIN

Prolactin is a hormone produced in the pituitary that stimulates the mammary glands to produce milk. Prolactin has other functions including an essential role in the maintenance of immune system functions. Prolactin levels rise during the latter part of pregnancy but the effects on lactation are suppressed by high levels of progesterone. Once progesterone drops at childbirth, milk secretion begins.

The second study below is interesting because it suggests that copper from a copper IUD can stimulate lactation. Whether it increases prolactin is unclear from the study but the possibility is there that copper causes an increase in prolactin production.

Prog Food Nutr Sci 1990;14(1):1-43

A review of the hormone prolactin during lactation.

Ostrom KM

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The principal lactogenic hormone, prolactin, secreted by the anterior pituitary is critical to the establishment of lactation, milk macronutrient content and milk production. The concentration of circulating prolactin increases during pregnancy so that by the end of gestation, levels are 10 to 20 times over normal amounts. However, prolactin is prevented from exerting its effect on milk secretion by elevated levels of progesterone. Following clearance of progesterone and estrogen at parturition, copious milk secretion begins. The minimal hormonal requirements for normal lactation to occur are prolactin, insulin and hydrocortisone. Prolactin stabilizes and promotes transcription of casein mRNA; may stimulate synthesis of alpha-lactalbumin, the regulatory protein of the lactose synthetase enzyme system; and increases lipoprotein lipase activity in the mammary gland. Prolactin levels decrease as lactation is established but nursing stimulates prolactin release from the pituitary which promotes continued milk production. Prolactin is secreted into milk at levels representative of the average circulating concentration. The physiological significance of milk prolactin to the infant is uncertain. Prolactin exists in three heterogenic forms which possess varying biological activity. The monomer with a molecular weight of 23 kDa is found in greatest quantity and is the principal biologically active form. The pattern of heterogeneity changes during pregnancy to favor even more monomer in proportion to the dimer. However, during lactation, the proportion of the monomer in circulation decreases in response to selective uptake of the monomer by the mammary gland. Over 90 percent of the prolactin in milk is present as the monomer. Prolactin may exert some of its biological effect by a shift in the ratio of active to less active forms of the molecule.

Title

Normoprolactinemic galactorrhea in a fertile woman with a **copper** intra-uterine device (**copper** IUD).

Author

Giampietro O; Ramacciotti C; Moggi G

Source

Acta Obstet Gynecol Scand, 63(1):23-5 1984

Abstract

We report a case of galactorrhea in a normoprolactinemic fertile woman (30 years old) wearing a **copper** intra-uterine device (Gravigard). The Gravigard was first inserted in July 1977. In February 1979 our patient noted spontaneous galactorrhea, mainly on the left, but it was also present on the right, after breast pressure. X-ray film of the sella turcica, visual-field examination, thyroid function and basal prolactin levels were all within normal limits. In May 1979 the Gravigard was withdrawn and milk loss stopped finally in December 1979. In March 1980 the IUD was replaced; after only 3 days, mild spontaneous lactation again ensued, on the right side. The patient never took drugs which might have occasioned a prolactin rise. Possible explanations for this unusual phenomenon are discussed.

J Exp Zool 2000 May;286(6):625-631

Direct influence of melatonin on the thyroid and comparison with prolactin.

Wright ML, Cuthbert KL, Donohue MJ, Solano SD, Proctor KL

Biology Department, College of Our Lady of the Elms, Chicopee, Massachusetts 01013.

[Record supplied by publisher]

Melatonin administered in vivo had previously been shown to inhibit thyroid cell proliferation and subsequent in vitro thyroxine (T(4)) secretion in anuran tadpoles. Melatonin in vitro also directly reduced the sensitivity of the thyroid to thyrotropin (TSH). The present work sought to determine whether melatonin directly affected baseline, unstimulated T(4) secretion, and to compare its effect with that of prolactin (PRL). Thyroids from larval *Rana catesbeiana* or adult *Rana pipiens* were incubated in control or melatonin (0.01 to 100 mug/ml) media. Melatonin directly inhibited T(4) secretion by thyroids from both tadpoles and frogs at all

concentrations of melatonin used and at both prometamorphic and climax tadpole stages. PRL, used in vitro at 10 mug/ml, did not influence the response of the thyroid to TSH (0.2 mug/ml) in young tadpoles, or the baseline secretion of T(4) by thyroids at any stage of larval life except climax, when T(4) secretion was significantly decreased by the third day of culture. Thus although both melatonin and PRL have been shown to antagonize the action of T(4) in vitro, and to decrease metamorphic rate, melatonin is a much more effective thyroid gland inhibitor than PRL. J. Exp. Zool. 286:625-631, 2000. Copyright 2000 Wiley-Liss, Inc.

Physiol Behav 2000 Jun 1-15;69(4-5):391-7

Hypothyroidism increases prolactin secretion and decreases the intromission threshold for induction of pseudopregnancy in adult female rats.

Tohei A, Taya K, Watanabe G, Voogt JL

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[Medline record in process]

In order to understand the mechanism by which thyroid hormones alter prolactin (PRL) secretion, we investigated the role of tuberoinfundibular dopamine (TIDA) neurons and pituitary and hypothalamus vasoactive intestinal peptide (VIP) in thiouracil- (0.03% in drinking water for 16 days) induced-hypothyroid adult female rats. The intromission threshold for induction of pseudopregnancy also was examined to evaluate the PRL response to coital stimulation in hypothyroid rats. Hypothyroidism in adult female rats did not affect TIDA neuronal activity as measured by tyrosine hydroxylase activity (DOPA accumulation 30 min after administration of m-hydroxybenzylhydrazine dihydrochloride, 100 mg/kg, i.p.) in the stalk-median eminence compared with that in euthyroid rats, whereas pituitary concentration of VIP was dramatically increased. Plasma concentration of PRL was higher at 1100 h of proestrus and estrus in hypothyroid rats as compared with that of euthyroid rats. The proportion of female rats exhibiting pseudopregnancy was higher in hypothyroid animals (100%) receiving seven intromissions than in euthyroid animals (43%). Administration of L-thyroxine in hypothyroid rats decreased the proportion of pseudopregnancy (40%) to the level of euthyroid animals. These results indicate that the increased level of pituitary VIP probably affects PRL secretion in a paracrine or autocrine manner and account for the hyperprolactinemia induced in hypothyroid female rats. No role for TIDA neurons in PRL elevation can be ascribed. A decrease in the intromission threshold for induction of pseudopregnancy might be due to increased levels of PRL in hypothyroid female rats.

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RAI or not RAI?

This is probably the hottest question on the treatment of Graves' Disease (hyperthyroidism) today.

RAI is RadioActive Iodine treatment in which the hyperthyroid patient is given a "cocktail" with radioactive iodine which goes to the thyroid and destroys much of its function.

Most doctors in the U.S. push RAI very heavily and try to get their patients to undergo it ASAP. Most doctors in Europe don't push RAI but favor maintenance on antithyroid drugs (ATDs) because of the high rate of "spontaneous" remissions and the possibility that RAI causes permanent damage to the body and may significantly increase the risk of cancer.

I think RAI is barbaric and insane and should never even be considered. Hopefully someday it will lie among the skeletons in the medical treatment closet. I also think that getting the radioiodine uptake test is a mistake and can cause damage to the thyroid and eyes. I really don't see the need for performing it.

The Atomic Women are a group of women (and hopefully some men) who have undergone RAI and now regret it. Read about their thoughts. New website (11-29-00) (<http://suite101.com/myhome.cfm/atomicwomen>)

Following is a quote from John Gofman. Please read his credentials because he is very knowledgeable about the use of radiation in medicine:

"In radiation research, nearly all the work is sponsored by the governments which are defending and promoting nuclear power . . . Ionizing radiation may well be the most important single cause of cancer, birth defects and genetic disorders . . . The stakes for human health are very, very high in radiation matters. It is essential that people take no chance that conflict-of-interest is producing radiation databases which cannot be trusted."

JOHN GOFMAN

John William Gofman is Professor Emeritus of Medical Physics at the University of California at Berkeley, and Lecturer at the Department of Medicine, University of California School of Medicine at San Francisco.

He is the author of several books and more than a hundred scientific papers in peer-review Journals, in the fields of nuclear/physical chemistry, coronary heart disease, ultracentrifugal analysis of the serum lipoproteins, the relationship of human chromosomes to cancer, and the biological effects of ionizing radiation with particular reference to cancer-induction.

In 1971 Gofman founded the Committee for Nuclear Responsibility, a small, non-profit, public interest association with three Nobel Laureates on its Board.

Among other Recent Honors and Awards, he received in December 1992, in Stockholm, Sweden: "The Right Livelihood Award" of the Right Livelihood Foundation, widely known as "The Alternative Nobel Prize".

Dr. Jakob von Uexkull's statement, in presenting the award for John Gofman's "pioneering work in exposing the health effects of low-level radiation," was:

"The Right Livelihood Award for vision and work forming an essential contribution to making life more whole, healing our planet, and uplifting humanity."

For more information on radiation, see:

<http://www.ratical.org/radiation/NRBE/NRBE8.html>

STUDIES:

Lancet 1999 Jun 19;353(9170):2111-5

Cancer incidence and mortality after radioiodine treatment for hyperthyroidism: a population-based cohort study.

Franklyn JA, Maisonneuve P, Sheppard M, Betteridge J, Boyle P

Department of Medicine, University of Birmingham, UK.

BACKGROUND: Radioiodine is used increasingly as first-line treatment for hyperthyroidism, but concerns remain about subsequent risk of cancer, especially in those treated at a young age. We investigated cancer incidence and mortality in patients treated with radioiodine for hyperthyroidism. **METHODS:** We did a population-based study in 7417 patients treated in Birmingham, UK, between 1950 and 1991. We compared details of all cancer diagnoses and deaths in 1971-91 from the UK Office for National Statistics with data on cancer incidence and mortality for England and Wales specific for age, sex, and period. **FINDINGS:** During 72,073 person-years of follow-up, 634 cancer diagnoses were made, compared with an expected number of 761 (standardised incidence ratio [SIR] 0.83 [95% CI 0.77-0.90]). The relative risk of cancer mortality was also decreased (observed cancer deaths 448, expected 499; standardised mortality ratio [SMR] 0.90 [0.82-0.98]). Incidence of cancers of the pancreas, bronchus, trachea, bladder, and lymphatic and haemopoietic systems was lowered. Mortality from cancers at all these sites was also reduced but findings were significant only for bronchus and trachea. There were significant increases in incidence and mortality for cancers of the small bowel (SIR 4.81 [2.16-10.72], SMR 7.03 [3.16-15.66]) and thyroid (SIR 3.25 [1.69-6.25], SMR 2.78 [1.16-6.67]), although absolute risk of these cancers was small. **INTERPRETATION:** The decrease in overall cancer incidence and mortality in those treated for hyperthyroidism with radioiodine is reassuring. The absolute risk of cancers of the small bowel and thyroid remain low, but the increased relative risk shows the need for long-term vigilance in those receiving radioiodine.

Comments:

- Comment in: Lancet 1999 Sep 25;354(9184):1122

PMID: 10382695, UI: 99310068

Success Rate of Radioiodine Therapy in Graves' Disease: The Influence of Thyrostatic Medication by Sabri O, Zimny M, Schulz G
J Clin Endocrinol Metab 84(4):1229-1234, April 1999

The usual treatment for Graves' disease is radioiodine (¹³¹I) therapy, but the use of thyrostatic medication with this therapy may decrease its effectiveness. This study attempted to determine the rate of effectiveness of ¹³¹I with and without concomitant use of carbimazole by prospectively studying 207 patients with Graves' disease. One hundred six patients were treated with ¹³¹I therapy and carbimazole and 101 were treated with ¹³¹I only. Patients were evaluated at 3, 6, and 12 months after therapy. The non-carbimazole group had a success (euthyroid 6 months after therapy) rate of 93% and the carbimazole group had a success rate of 49%. Logistic regression indicated that there was an association between failure and the administration and dose of carbimazole despite the increased dose of ¹³¹I when given carbimazole.

Acta Endocrinol (Copenh) 1990 Feb;122(2):233-40

Peripheral blood T cell activation after radioiodine treatment for Graves' disease.

Teng WP, Stark R, Munro AJ, Young SM, Borysiewicz LK, Weetman AP

Department of Medicine, University of Cambridge Clinical School, Addenbrooke's Hospital, UK.

Radioiodine therapy for Graves' thyrotoxicosis produces a rise in thyroid autoantibodies in the first three months after treatment, but little is known of its effects on T cells. We have therefore followed the changes in T cell subsets in sequential samples from 23 patients with Graves' disease treated with radioiodine, using dual-colour flow cytometry. In the first month after treatment there was a significant rise in activated T cells, identified by the markers HLA-DR (Ia) and CDw26/Ta1 (p less than 0.025 in both cases). CD45RO-positive T cells, which are the primed population containing memory cells, also increased (p less than 0.025), but there was no change in CD45R-positive, resting T cells or in the CD4 to CD8 (helper to cytotoxic/suppressor) ratio. Vicia villosa-binding T cells, containing the contrasuppressor population, showed a more variable response, but the trend was to an overall increase from pre-treatment values (p less than 0.025). The changes did not appear to be related to antithyroid drug treatment, since they were seen irrespective of whether patients continued such therapy. These results suggest that T cell activation and enhanced contrasuppressor activity may in part be responsible for the rise in autoantibodies after radioiodine. The T cell changes could also contribute to the worsening of ophthalmopathy seen in some radioiodine-treated patients.

PMID: 2316311, UI: 90195418

The following letter is from: daisy@gemstate.net (Elaine Moore)

If you're thinking of becoming pregnant, you don't want to have RAI. Recent studies show that chromosomal changes caused by radioiodine can be passed to the next generation. Like DES and other hormonal disruptors, the effects are stronger and more significant when passed on to children, and often, these changes aren't evident for 30 years or so. Also, several recent studies show a slight but significant risk of increased cancer mortality for several types of cancer in patients who had RAI. I had RAI which I regret and now have an atrophied pancreas. One study shows an increase of pancreatic cancer after RAI.

Also, the antibodies which increase after RAI persist for years and may be transferred to the fetus, causing transient thyroid problems.

Eleven years after RAI, I have high levels of thyroid antibodies and mitochondrial antibodies. See Dr. Stoll's site for examples of what happens when you don't address the underlying causes of autoimmunity. Remember, the thyroid is the victim, not the cause.

You do, however, need to get your thyroid levels under control before you become pregnant since there is a chance that your symptoms will worsen in early pregnancy and in the postpartum period. For the most part, pregnancy brings relief of symptoms since there's immune system suppression.

ATD's can be used during pregnancy, but there is a slight risk of fetal hypothyroidism, especially with Tapazole. If you can at least lower your dose, it would help, and there are many things you can do to help in this regard. Diet and stress reduction seem to be the most important. Eat plenty of goitrogens, foods which act like ATD's (cabbage, cauliflower, almonds, peaches, soy, peanuts, etc.) Reduce your dairy, saturated fats, sugar, and iodine. GD is associated with many nutrient deficiencies, particularly free fatty acids, vitamins C, E, B, copper, magnesium, etc. See John's supplement list on this site.

Stress reduction methods, either meditation, tai chi, or yoga and energy healing, like acupuncture, etc. are all of great value. Sometimes, though, there's lots of stress involved with trying to get everything right. Then, surgery is a viable option if your symptoms seem to be life threatening. By the way, your levels are high but not extremely high. What's important, though, is how much they have changed and if you're seeing improvement with your ATD's.

Following is a great, must-read historical review of the use of radiation in medicine. It's an unbelievable history and it makes you not want to be a part of it.

From: j_alicia39@hotmail.com (Julia)

Hi you all,

The long paper below, might seem being out of track at a hyperthyroidism board. But those considering RAI or already RAI'ed are couteously suggested to read it carefully. Some of the data it contains have sometimes been quoted at our atomicwomen mailing-list and yahoo club. (links at the bottom). Drs. Wood, Cooper and Rigdeway, in their book "Your thyroid a home reference", quote how over 2.000.000.- children and adolescents in USA were given X-rays between 1920's and 1960's for problems like enlarged tonsils or adenoids, birthmarks, whooping cough, acne and ringworm of the scalp. They add: ""Subsequent large-scale studies of thyroid cancer frequency in radiated and non radiated control groups have established beyond doubt the relationship between radiation exposure and thyroid cancer"".

Julia

The Major Cause Of Cancer, Part 1
Rachel's Environment And Health Weekly #691 3-21-00

When Wilhelm Roentgen first discovered X-rays, in 1895, "doctors and physicians saw the practical potential of X-rays at once, and rushed to experiment with them." [1,pg.7] Many physicians built their own X-ray equipment, with mixed results: some home-brew X-ray machines produced no radiation whatsoever, others produced enough to irradiate everyone in the next room.

The ability to see inside the human body for the first time was a marvelous, mysterious and deeply provocative discovery. Roentgen trained X-rays on his wife's hand for 15 minutes, producing a macabre image of the bones of her hand adorned by her wedding ring. Roentgen's biographer, Otto Glasser, says Mrs. Roentgen "could hardly believe that this bony hand was her own and shuddered at the thought that she was seeing her skeleton. To Mrs. Roentgen, as to many others later, this experience gave a vague premonition of death," Glasser wrote.[1,pg.4]

Within a year, by 1896, physicians were using X-rays for diagnosis and as a new way of gathering evidence to protect themselves against malpractice suits. Almost immediately -- during 1895-96 -- it also became clear that X-rays could cause serious medical problems. Some physicians received burns that wouldn't heal, requiring amputation of their fingers. Others developed fatal cancers.

At that time, antibiotics had not yet been discovered, so physicians had only a small number of treatments they could offer their patients; X-rays gave them a range of new procedures that were very "high tech" -- bordering on the miraculous -- and which seemed to hold out promise to the sick. Thus the medical world embraced these mysterious, invisible rays with great enthusiasm. Understandably, physicians at the time often thought they observed therapeutic benefits where controlled experiments today find none.

At that time -- just prior to 1920 -- the editor of AMERICAN X-RAY JOURNAL said "there are about 100 named diseases that yield favorably to X-ray treatment." In her informative history of the technology, MULTIPLE EXPOSURES; CHRONICLES OF THE RADIATION AGE, Catherine Caufield (see REHW #200, #201, #202), comments on this period: "Radiation treatment for benign [non-cancer] diseases became a medical craze that lasted for 40 or more years." [1,pg.15] "...[L]arge groups of people [were] needlessly irradiated for such minor problems as ringworm and acne.... Many women had their ovaries irradiated as a treatment for depression." [1,pg.15] Such uses of X-rays would today be viewed as quackery, but many of them were accepted medical practice into the 1950s. Physicians weren't the only ones enthusiastic about X-ray therapies. If you get a large enough dose of X-rays your hair falls out, so "beauty shops installed X-ray equipment to remove their customers' unwanted facial and body hair," Catherine Caufield reports.[1,pg.15]

Roentgen's discovery of X-rays in 1895 led directly to Henri Becquerel's discovery of the radioactivity of uranium in 1896 and then to the discovery of radium by Marie Curie and her husband Pierre in 1898, for which Becquerel and the Curies were jointly awarded the Nobel prize in 1903. (Twenty years later Madame Curie would die of acute lymphoblastic leukemia.)

Soon radioactive radium was being prescribed by physicians alongside X-rays. Radium treatments were prescribed for heart trouble, impotence, ulcers, depression, arthritis, cancer, high blood pressure, blindness and tuberculosis, among other ailments. Soon radioactive toothpaste was being marketed, then radioactive skin cream. In Germany, chocolate bars containing radium were sold as a "rejuvenator." [1,pg.28] In the U.S., hundreds of thousands of people began drinking bottled water laced with radium, as a general elixir known popularly as "liquid sunshine." As recently as 1952 LIFE magazine wrote about the beneficial effects of inhaling radioactive radon gas in deep mines. Even today The Merry Widow Health Mine near Butte, Montana and the Sunshine Radon Health Mine nearby advertise that visitors to the mines report multiple

benefits from inhaling radioactive radon,[2] even though numerous studies now indicate that the only demonstrable health effect of radon gas is lung cancer.

Thus the medical world and popular culture together embraced X-rays (and other radioactive emanations) as miraculous remedies, gifts to humanity from the foremost geniuses of an inventive age.

In the popular imagination, these technologies suffered a serious setback when atomic bombs were detonated over Japan in 1945. Even though the A-bombs arguably shortened WW II and saved American lives, John Hersey's description of the human devastation in HIROSHIMA forever imprinted the mushroom cloud in the popular mind as an omen of unutterable ruin. Despite substantial efforts to cast The Bomb in a positive light, radiation technology would never recover the luster it had gained before WW II.

Seven years after A-bombs were used in war, Dwight Eisenhower set the U.S. government on a new course, intended to show the world that nuclear weapons, radioactivity and radiation were not harbingers of death but were in fact powerful, benign servants offering almost-limitless benefits to humankind. The "Atoms for Peace" program was born, explicitly aimed at convincing Americans and the world that these new technologies were full of hope, and that nuclear power reactors should be developed with tax dollars to generate electricity. The promise of this newest technical advance seemed too good to be true -- electricity "too cheap to meter." [3]

The Atomic Energy Act of 1946 created the civilian Atomic Energy Commission but as a practical matter the nation's top military commanders maintained close control over the development of all nuclear technologies.[4]

Thus by a series of historical accidents, all of the major sources of ionizing radiation fell under the purview of people and institutions who had no reason to want to explore the early knowledge that radiation was harmful. In 1927, Hermann J. Muller had demonstrated that X-rays caused inheritable genetic damage, and he received a Nobel prize for his efforts. However, he had performed his experiments on fruit flies and it was easy, or at least convenient, to dismiss his findings as irrelevant to humans.

In sum, to physicians, radiation seemed a promising new therapy for treating nearly every ailment under the sun; for the military and the Joint Commission on Atomic Energy in Congress it unleashed hundreds of billions of dollars, a veritable flood of taxpayer funds, most of which came with almost no oversight because of official secrecy surrounding weapons development; and for private-sector government contractors like Union Carbide, Monsanto Chemical Co., General Electric, Bechtel Corporation, DuPont, Martin Marietta and others -- it meant an opportunity to join the elite "military-industrial complex" whose growing political power President Eisenhower warned against in his final address to Congress in 1959.

Throughout the 1950s the military detonated A-bombs above-ground at the Nevada Test Site, showering downwind civilian populations with radioactivity.[5] At the Hanford Reservation in Washington state, technicians intentionally released huge clouds of radioactivity to see what would happen to the human populations thus exposed. In one Hanford experiment 500,000 Curies of radioactive iodine were released; iodine collects in the human thyroid gland. The victims of this experiment, mostly Native Americans, were not told about it for 45 years.[6,pg.96] American sailors on ships and soldiers on the ground were exposed to large doses of radioactivity just to see what would happen to them. The military brass insisted that being showered with radiation is harmless.

In his autobiography, Karl Z. Morgan, who served as radiation safety director at the Oak Ridge National Laboratory (Clinton, Tennessee) from 1944 to 1971, recalls that, "The Veterans Administration seems always on the defensive to make sure the victims are not compensated." [6,pg.101] Morgan recounts the story of John D. Smitherman, a Navy man who received large doses of radiation during A-bomb experiments on Bikini Atoll in 1946. Morgan writes, "The Veterans Administration denied any connection to radiation exposure until 1988, when it had awarded his widow benefits. By the time of his death, Smitherman's body was almost consumed by cancers of the lung, bronchial lymph nodes, diaphragm, spleen, pancreas, intestines, stomach, liver, and adrenal glands. In 1989, a year after it had awarded the benefits, the VA revoked them from Smitherman's widow." [6,pg.101]

Starting in the 1940s and continuing into the 1960s, thousands of uranium miners were told that breathing radon gas in the uranium mines of New Mexico was perfectly safe. Only now are the radon-caused lung cancers being tallied up, as the truth leaks out 50 years too late.

In retrospect, a kind of nuclear mania swept the industrial world. What biotechnology and high-tech computers are today, atomic technology was in the 1950s and early 1960s. Government contractors spent billions to develop a nuclear-powered airplane -- even though simple engineering calculations told them early in the project that such a plane would be too heavy to carry a useful cargo.[4,pg.204] Monsanto Research Corporation proposed a plutonium-powered coffee pot that would boil water for 100 years without a refueling.[4,pg.227] A Boston company proposed cufflinks made of radioactive uranium for the simple reason that uranium is heavier than lead and "the unusual weight prevents cuffs from riding up." [4,pg.227]

In 1957, the Atomic Energy Commission established its Plowshare Division -- named of course for the Biblical "swords into plowshares" phrasing in Isaiah (2:4).[4,pg.231] Our government and its industrial partners were determined to show the world that this technology was benign, no matter what the facts might be. On July 14, 1958, Dr. Edward Teller, the father of the H-bomb, arrived in Alaska to announce Project Chariot, a plan to carve a new harbor out of the Alaska coast by detonating up to six H-bombs. After a tremendous political fight -- documented in Dan O'Neill's book, THE FIRECRACKER BOYS[7] -- the plan was shelved. Another plan was developed to blast a new canal across Central America with atomic bombs, simply to give the U.S. some leverage in negotiating with Panama over control of the Panama Canal. That plan, too, was scrapped. In 1967, an A-bomb was detonated underground in New Mexico, to release natural gas trapped in shale rock formations. Trapped gas was in fact released, but -- as the project's engineers should have been able to predict -- the gas turned out to be radioactive so the hole in the ground was plugged and a bronze plaque in the desert is all that remains visible of Project Gasbuggy.[4,pg.236]

In sum, according to NEW YORK TIMES columnist H. Peter Metzger, the Atomic Energy Commission wasted billions of dollars on "crackpot schemes," all for the purpose of proving that nuclear technology is beneficial and not in any way harmful.[4,pg.237]

The Plowshare Division may have been a complete failure, but one lasting result emerged from all these efforts: A powerful culture of denial sunk deep roots into the heart of scientific and industrial America.

[To be continued April 13.]

Descriptor terms: radiation; nuclear weapons; nuclear power; x-rays; cancer; carcinogens; karl z. morgan; downwinders; nevada test site; hanford;

===== [1] Catherine Caufield, MULTIPLE EXPOSURES; CHRONICLES OF THE RADIATION AGE (New York: Harper & Row, 1989). ISBN [2] Jim Robbins, "Camping Out in the Merry Widow Mine," HIGH COUNTRY NEWS Vol. 26, No. 12 (June 27, 1994), pgs. unknown. See <http://www.hcn.org/1994/jun27/dir/reporters.html>. And see <http://www.roadsideamerica.com/attract/MTBASradon.html> [3] Arjun Makhijani and Scott Saleska, THE NUCLEAR POWER DECEPTION; U.S. NUCLEAR MYTHOLOGY FROM ELECTRICITY "TOO CHEAP TO METER" TO "INHERENTLY SAFE" REACTORS (New York: The Apex Press, 1999). ISBN 0-945257-75-9. [4] H. Peter Metzger, THE ATOMIC ESTABLISHMENT (New York: Simon & Schuster, 1972). ISBN 671-21351-2. [5] Michael D'Antonio, ATOMIC HARVEST (New York: Crown Publishers, 1993). ISBN 0-517-58981-8. And: Chip Ward, Canaries on the Rim: Living Downwind in the West (New York: Verso, 1999). ISBN 1859847501. [6] Karl Z. Morgan and Ken M. Peterson, THE ANGRY GENIE; ONE MAN'S WALK THROUGH THE NUCLEAR AGE (Norman, Oklahoma: University of Oklahoma Press, 1999). ISBN 0-8061-3122-5. [7] Dan O'Neill, THE FIRECRACKER BOYS (New York: St. Martin's Press, 1994). ISBN 0-312-13416-9.

Some lines from "Your thyroid", by Dr Lawrence Wood et al.: In the 1920's physicians began to use radiation (X rays) to treat non cancerous disorders. One of the more common problems that was treated in this manner was an enlargement of the thymus gland in newborns. The thymus gland is located behind the breastbone and is important for normal immune function.

Other conditions treated in this manner included enlarged tonsils or adenoids, birthmarks, whooping cough, acne, and ringworm of the scalp. Treatment was given by means of an X-ray machine ("external beam irradiation") or by placing radioactive material, such as radium, directly in or on the tissue to be treated. For many years radiation was considered good medical therapy for some of these problems. For example deafness was improved when radium treatments shrank enlarged lymph tissue compressing the internal ear canal. Acne could be markedly improved by radiation, resulting in less facial scarring.

In short, radiation therapy was used because it seemed safe and effective. Unfortunately the thyroid gland, located as it is in front of the neck, often received radiation inadvertently during treatment for these conditions. In the 1950's physicians began to notice an increased number of benign and malignant thyroid tumors among patients who had been given radiation therapy years earlier. The fact that the radiation had caused the thyroid tumors was substantiated when it was found that many individuals exposed to atomic-bomb radiation or fallout also developed thyroid tumors in later years. When these facts became known, these forms of radiation therapy were of course discontinued.

Nevertheless it is estimated that two million people in the United States received radiation treatments in childhood or adolescence between 1920 and the early 1960s. Subsequent large-scale studies of thyroid-cancer frequency in radiated and nonradiated control groups have established beyond doubt the relationship between radiation exposure and thyroid cancer.

Subj: [hyperthyroidism] Re: Back to the Basics -- (Again)

Date: 1/31/00 8:16:19 PM !!!First Boot!!!

From: j_alicia39@hotmail.com (julia c amado)

Reply-to: hyperthyroidism@egroups.com

To: hyperthyroidism@egroups.com

>From: Doug

Date: Wed, 16 Feb 2000 20:13:56 -0500

Dear AntJoan,

In your previous message to Mary, you wrote: "RAI seems to cause a lot of problems down the road, which the doctors don't warn us about." Can you send us a pretty comprehensive list of problems? Our doctors say that by taking synthoid, life returns to normal forever. What do you know that they're not telling?

Doug

Hi Doug,

I got ophthalmopathy ten months after having RAI. I was not even warned about the possibility!. I did not have ophthalmopathy prior RAI, but developed it some 10 months later, and was clearly induced by it. Although there are endos that don't relate TAO/TED to RAI, most of them accept it does.

The current (1998) edition of Williams' Textbook of Clinical Endocrinology states that RAI is responsible for the development of TED and pretibial myxedema and exacerbates these conditions when they're already present. Current medical books are now listing ATDs as the treatment of choice. The Williams Text had already demoted RAI from first place, back in 1994, but found occasions where it was the best choice, f.i. for patients allergic to ATDs who are poor surgical candidates, (2nd choice after ATDs) due to advanced age or a coexisting disease making these patients a surgical risk. An article in the New England Journal of Medicine (Jan 8, 1998--Vol. 338, No. 2) that studied the occurrence of TED after RAI showed in its results that 15% of the 150 treated with RAI developed or worsened the TED. The patient's they studied had slight or NO TED before having the RAI. With the group that took the RAI and steroids (145 patients) 50 of the 75 that had TED had improvement and NO patient had progression.

DeGroot et al quote:

"I131 therapy causes an increase in titers of TSH-RABs, and anti-TG or TPO antibodies, which reflects an activation of autoimmunity. It probably is due to release of thyroid antigens by cell damage, or destruction of intrathyroidal T cells. "Although completely satisfactory statistical proof is lacking, many thyroidologists are convinced that I131 therapy can lead to exacerbation of infiltrative ophthalmopathy, perhaps because of this immunologic response. "Tallstedt and associates have published data indicating that I131-I therapy causes exacerbation of ophthalmopathy in nearly 25% of patients, while surgery is followed by this response in about half as many. Thus, as described below, patients with significant ophthalmopathy may receive corticosteroids along with I131, or may be selected for surgical management."

More:

A study in the Lancet Journal of Medicine from June 1999 reports that those of us who had RAI have a significantly higher incidence of thyroid and small bowel cancer. That is not strange: guts and thyroid share the same embryogenic origin. This subject had been already reported at The New England Journal of Medicine -- March 12, 1998 -- Vol. 338, No. 11, whose study was conducted in a cohort of 7209 subjects with hyperthyroidism, treated with radioactive iodine between 1950 and 1989, which is certainly a high figure of people for these kind of studies in a rare disease like ours. Not to speak about radiation received by other organs, germinal cells included. And all related to becoming hypo after RAI, increasing each year and reaching 80% of cases ten years later.

It's good another RAI group has been created. The more the better, to get the word out and help people to take as informed decisions as possible. As I've already announced here, yet there is a yahoo club founded on Jan 6th.

Those interested can join it at <http://clubs.yahoo.com/clubs/atomicwomen>.

More from Julia:

Radioactivity only mutates and lately kills cells, so regretfully radiation doesn't cure anything. It's only mutagenic, many mutations leading to cancers. One can ask, why is it then used against cancer when it actually produces it?. Because of its stochastic effects. And what does this mean?. Stochastic effects are effects that occur on a random basis with its effect being independent of the size of dose. The effect typically has no threshold and is based on probabilities, with the chances of seeing the effect increasing with dose. Cancer is thought to be a stochastic effect. So doctors use *high* doses of radioactivity against a tumor, considering that this will surpass the stochastic effects.

Graves' is not cured either. It destroys, damages tissue, thus with less thyroid cells to produce hormones, fewer hyper symptoms. This is what doctors think, ...as they also think that after words "hypo is easier to control", "one pill a day and you'll be OK", "T4 is exactly the same hormone your body produces" and "it's all in your head".

These are official medical DOGMAS that we, iatrogenic (i.e. medically caused) hypothyroid know by heart.

So, doses used for Graves' don't ablate the gland, like in thyroid cancer, but partially destroy its tissues. The destruction is achieved with beta particles and high energy gamma radiation emitted by I-131 on its decay.

And the amount of tissue actually destroyed depends on several factors:

- iodine uptake by the gland
- bulk of tissue to be destroyed
- length of time radioactive iodine is retained in the gland
- distribution within the tissue
- radiosensitivity of thyroid cells
- dose
- high iodine diet can interfere
- different opinions re. Thyroid blockers role
- degree of hyperthyroidism, etc

Many factors depend on the characteristics of the gland, that differ among individuals. Given dose is also important, because it's often very badly calculated. How many people have an eco-doppler study done prior RAI?. Almost nobody!. How many have a iodine uptake prior RAI?. Very few. More often than not, doses are given on an "estimation" basis upon a supposed weight of gland. And even two or three protocols, depending on the dose, but there are a number of doctors who opt for dosing at large to ensure quick hypothyroidism.

Among those who use lower doses, RAI doesn't instantaneously eradicate the thyroid. It's a process that continues to progress over several years. There may be a small number of patients that don't become hypothyroid immediately, but it's been proven that, within 10 years after RAI, 100% of RAI'ed people is hypothyroid.

I know of some persons who feel better 1, 2 or 3 years after RAI, specially because they feel relieved from hyper symptoms. I don't want to rain over other's parade, but as soon as hypothyroidism is present, most of them invariably miss and long for their old hyper days.

There is some more information at AtomicWomen's site. You might consider visiting it here:

<http://www.suite101.com/myhome.cfm/atomicwomen>

Regards

Julia

From About.com May 30, 2000:

RADIATION DAMAGE MAY BE PASSED TO OFFSPRING

According to researchers in the UK and Russia, reporting in the May 4, 2000 issue of "Nature," the dangerous health impact of radiation may be passed down from one generation to the next. The study of mice found that offspring of mice exposed to radiation had an increased number of genetic mutations, as did their offspring--even though the two generations of younger mice had not been exposed to radiation. The research indicates that some radiation effects may be delayed, leading to genetic disorders years or decades after exposure. (Source: Nature 2000;405:37.)

July 6, 2000

I don't know if doctors get an actual kickback, but RAI has such bad side effects, including rendering the patient hypo for life, that the doctor has a patient for life--lots of guaranteed income. I am SO GLAD that I listened to my own instincts, and not the idiot endo, and did not destroy my thyroid. So much of the time Graves disease goes into remission all by itself--why wouldn't anyone just go on meds and explore alternate healing, rather than opt for a "final solution," which is no solution at all, as you will end up sicker than when you started? I am certainly not upset about hurting the poor doctor's feelings w/all of my questions and opinions--I have only one body, and one life, which are entrusted to me to care for and save, and are SO MUCH more important than the doctor's ego. Let's see--weigh the doctor's need to feel like he is playing God and is all-knowing against my need to survive and be healthy. I don't really see a choice here. AntJoan

Subj: [hyperthyroidism] Re: WHY?!?! RAI better than surgery?!?!
Date: 7/7/00

From: tnccline@nemonet.com (Christine Cline)

The following is an excerpt from an American medical journal. It shows the difference between the American doctors' way of thinking compared to other countries. It also points out there is a 40 to 50 percent remission rate with ATD's.

The New England Journal of Medicine -- January 25, 1996 -- Vol. 334, No. 4

Immunosuppression of Graves' Hyperthyroidism -- Still an Elusive Goal

Fifty years have passed since radioactive iodine and antithyroid drugs became available for the treatment of hyperthyroidism caused by Graves' disease. Despite the efficacy of both treatments, opinions still diverge widely as to which is better. A course of antithyroid-drug therapy requires prolonged daily treatment, but 40 to 50 percent of patients treated for a year remain euthyroid after therapy is discontinued. Therapy with iodine-131, on the other hand, is simple and fast (one dose usually suffices), but the treatment causes hypothyroidism in a large proportion of patients. In a survey of endocrinologists, 69 percent of the responding physicians in the United States preferred iodine-131 for the treatment of a typical patient with Graves' hyperthyroidism, but an antithyroid drug was preferred by 77 percent of the respondents in Europe and by 88percent in Japan. (1) Obviously, doctors in the United States are disappointed by the high rate of recurrence of hyperthyroidism after the discontinuation of antithyroid-drug therapy, whereas those in Europe and Japan are more inclined to give the patient a chance to have a spontaneous remission, thereby avoiding lifelong treatment with thyroxine (T4).

>>>>The entire article can be found at the following:

<http://www.nejm.org/content/1996/0334/0004/0265.asp>

Subj: RAI

Date: 9/2/00 2:41:22 AM Pacific Daylight Time

From: MsSlipper@aol.com

Reply-to: hyperthyroidism@egroups.com

To: hyperthyroidism@egroups.com

Hi,

Haven't written in awhile but am having lots of difficulties. Had RAI in 1996 for Toxic Multi-nodular Goiter. Was on PTU for a few months previous to RAI and started to feel better then I had in years. After RAI I have never felt well. I have developed double vision in my eyes which is due to a muscular problem (I'm told) they hurt all the time and my lids are puffy and feel like they have sand under them. My optometrist won't renew my eye glasses until the problem is fixed. If I read or drive the problem gets worse. My primary care doc had a CAT scan of my head done, which was fine, I was then referred to a neurologist who did an MRI and that was fine. He did blood work too and found my TSH was .3 My primary then reduced my Levoxyl to .75 mcg. from .88 mcg She then sent me to an endo doc who swore I am not hyper thyroid again nor could the nodules have grown back, because RAI makes the thyroid atrophy. She said is unlikely my eye problem has any connection to my thyroid, or medication because only Graves patients get eye problems. She did however do a thyroid antibody test (I have never had one before) just in case I could have Graves as well as having Toxic Multi-Nodular.

For one I am sorry I ever had RAI. I have also developed high blood pressure in the last two years which I NEVER NEVER had. I am either hanging off the ceiling or don't have the pep to tie my sneakers. Anyone out there feel similar? People are right, read, read, read before you make a decision.

From Zoey:

In May I was diagnosed with HyperT and Graves. 5 Docs(3 endos and 2 internists) urged me to have RAI - the only thing that would work. I told them RAI was not an option. I began taking 20 mgs of Tapazole a day (which was considerably less than they recommended) and within 3 weeks my T4, T3, TSH, etc. were at the lower (hypo) end of normal range. For the past 2 months or so I have been taking only 2 1/2 mgs of Tapazole a day and my bloodwork has been stable, normal, and euthyroid. The doctors told me only RAI would work. I am so thankful I didn't listen to them. I hope you will take some time to consider your options. Destroying your thyroid gland is final and frequently causes more problems than it corrects. Please let us know your decision. with all my best, Zoey

New insights into pathogenesis and potential therapeutic options for Graves orbitopathy.

Warwar RE

Department of Ophthalmology, Wright State University School of Medicine, Dayton, Ohio 45429, USA.

Graves disease is an autoimmune disorder that affects the seemingly heterogeneous tissues of the thyroid and orbit. Evidence suggests that these tissues share a common antigen: the thyroid-stimulating hormone receptor protein. It is speculated that this antigen (which is present in orbital tissue in both normal patients and patients with Graves disease), together with the humoral factors present in the serum of patients with Graves disease, forms the basis for the immunologic attack seen in Graves ophthalmopathy. Once the immune response has been activated, a series of pro-inflammatory cytokines propagate inflammation, leading to the clinical findings typical of Graves ophthalmopathy. Knowledge of the specific inflammatory mediators involved may someday lead to the development of specific, clinically available immunomodulatory therapies for Graves eye disease.

Lancet 2000 Apr 29;355(9214):1505-9

Radiotherapy for Graves' orbitopathy: randomised placebo-controlled study.

Mourits MP, van Kempen-Harteveld ML, Garcia MB, Koppeschaar HP, Tick L, Terwee CB

Donders Institute of Ophthalmology (Orbital Unit), University Medical Centre, Utrecht, The Netherlands.

BACKGROUND: The best treatment (steroids, irradiation, or both) for moderately severe Graves' orbitopathy, a self-limiting disease is not known. We tested the efficacy of external beam irradiation compared with sham-irradiation. **METHODS:** In a double-blind randomised clinical trial, 30 patients with moderately severe Graves' orbitopathy had radiotherapy (20 Gy in ten fractions), and 30 were assigned sham-irradiation (ten fractions of 0 Gy). Treatment outcome was measured qualitatively by changes in major and minor criteria and quantitatively in several ophthalmic and other variables, such as eyelid aperture, proptosis, eye movements, subjective eye score, and clinical-activity score at 24 weeks. **FINDINGS:** The qualitative treatment outcome was successful in 18 of 30 (60%) irradiated patients versus nine of 29 (31%) sham-irradiated patients at week 24 (relative risk [RR]=1.9 [95% CI 1.0-3.6], $p=0.04$). This difference was caused by improvements in diplopia grade, but not by reduction of proptosis, nor of eyelid swelling. Quantitatively, elevation improved significantly in the radiotherapy group, whereas all other variables remained unchanged. The field of binocular single vision was enlarged in 11 of 17 patients after irradiation compared with two of 15 after sham-irradiation. Nevertheless, only 25% of the irradiated patients were spared from additional strabismus surgery. **INTERPRETATION:** In these patients with moderately severe Graves' orbitopathy, radiotherapy should be used only to treat motility impairment.

From: mhorten@nctsi.navy.mil (Horten, Mona)

Good morning....last night a neighbor came over and we chatted while handing out candy to the trick-or-treaters. He was rendered hypo several years ago. He had RAI. They never bothered to try any of the ATDs. Now he is always tired, hasn't slept well since RAI and when he gets sick, he stays sicker longer. He also told me since the RAI his saliva has changed and he can't lick an envelope or stamp because they won't stay stuck! Weird huh? I have also noticed he seems "down" lately. I think his thyroid levels are off so he's going in for blood work. He hates the way he feels! He's 39 years old and likes all kinds of outdoor activities with his kids and wishes he felt better. He also told me it took OVER A YEAR before the thyroid was destroyed and in the meantime had to take meds. Just thought I'd share this. Mona

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RUBIDIUM

Rough file:

"The distribution of calcium, copper, and zinc in urine varied among individuals with primary tumors; however, **rubidium** levels tended to be consistently elevated. An attempt is being made to correlate these various differences with the extent of the primary disease at the time of surgery, the postoperative tumor-free interval, and subsequent therapy." [rubidium high in cancerous breast tissue.doc](#)

"Compared to the rats fed the diet with supplemental **rubidium**, the animals fed the diet without **rubidium** supplementation had higher urea nitrogen in plasma; lower **rubidium** concentration in tissues; lower sodium in muscle; higher potassium in plasma, kidney and tibia, and lower potassium in testis; lower phosphorus in heart and spleen; lower calcium in spleen; higher magnesium in muscle and tibia; higher iron in muscle; lower zinc in plasma and testis; and lower copper in heart, liver, and spleen, and higher copper in kidney. These results suggest that **rubidium** concentration in tissues reflects **rubidium** intake, and that **rubidium** depletion affects mineral (sodium, potassium, phosphorus, calcium, magnesium, iron, zinc, and copper) status." [rubidium--deficiency effects.doc](#)

"Simultaneous supplementation of copper with selenite or selenate at the described levels has a profound influence on the concentration levels of other elements in the normal as well as in the diseased mice. The administration of selenium (0.67 micrograms/g body wt sodium selenite or sodium selenate, daily) and selenium and copper (0.67 and 1.35 micrograms/g body wt, respectively) has no effect on the incidence rate of hepatoma development." [rubidium--effects of copper and selenium.doc](#)

"Sodium and potassium are two essential alkali metals in man. Lithium is used as therapeutic agent in bipolar affective disorders. **Rubidium** has been investigated for its antidepressant effect in a group of psychiatric disorders. Cesium is under laboratory investigation for its role in carcinogenesis and in depressive illness. Very little is known of francium due to its great instability for experimental study." [rubidium and cesium--antidepressant effects.doc](#)

"**rubidium**-treated rats excreted potassium at a much higher rate of 14.6 +/- 3.0%. The potassium content of principal cells was, however, significantly lower in **rubidium**-treated than in potassium-deprived animals. Similar to experiments in which **rubidium** was given acutely (3 hours), chronic **rubidium** administration was associated with preferential accumulation of **rubidium** in all tubule cells relative to potassium. **Rubidium** clearances were uniformly below those of potassium. Amiloride abolished the difference between **rubidium** and potassium clearances and sharply reduced the excretion of both cations. In view of the known site of action of amiloride, this suggests a distal tubule site of **rubidium** action on potassium transport. Amiloride also reduced or abolished the preferential uptake of **rubidium** into all but intercalated tubule cells. Marked cell heterogeneity of **rubidium** accumulation into intercalated cells was observed: One subpopulation, with low cell chloride, retained **rubidium** more effectively than another subpopulation with high cell chloride." [rubidium induced kaluresis.mechanism of action.doc](#)

"Male and female Sprague-Dawley rats were fed purified diets in which the carbohydrate component was either starch or refined sugar (sucrose). The addition to these diets of the ash prepared by the incineration of unrefined muscovado sugar prevented the deficiencies of Factor R seen in the offspring when the diets were not supplemented with ash. Analysis by neutron activation showed that the ash from the unrefined sugar significantly increased the proportion of iron, cobalt, manganese, caesium and **rubidium** in the diets. The addition of chlorides of all five mineral elements to the diet containing refined sugar also prevented the development of signs of deficiency of Factor R in the pups. However the addition of cobalt chloride alone, or of cobalt and manganese chlorides, did not prevent the deficiency. It is likely that what we have called reproductive Factor R is iron, caesium or **rubidium**." [rubidium and cesium may be essential for life.doc](#)

"The role of reduced glutathione (GSH) in lens membrane function was studied by depleting GSH with 1-chloro-2,4-dinitrobenzene (CDNB), a reaction catalyzed by GSH-S-transferase. Depletion of GSH in the lens epithelium by 70-90% led to a decrease in uptake and increase in efflux of ⁸⁶Rb. It is concluded that deficiency of GSH causes a marked increase in membrane permeability and such lenses are susceptible to oxidative damage resulting in inactivation of the Na⁺/K⁺ pump, thus leading to ionic changes and cataract development." [rubidium uptake decreased by gsh deficiency.doc](#)

"Lithium chloride and **rubidium** chloride were tested under conditions in which the effects of their chronic administration on aversively-controlled behavior could be assessed. Lithium attenuated shock-induced suppression of open-field activity when that suppression was under the control of mild or moderate stimulus parameters, but had no effect on the suppression produced by the presence of shock itself. **Rubidium**, on the other hand, increased shock-induced suppression under all conditions. When shock was removed and extinction of the activity suppression was investigated, lithium subjects failed to return to their original baseline activity levels, while subjects receiving **rubidium** recovered baselines in a manner indistinguishable from that observed in control animals." [rubidium and lithium effects on fear.doc](#)

"LiCl and RbCl added in vitro at concentration of 0.01 mM increased significantly platelet GABA binding." [rubidium and lithium increase GABA binding.doc](#)

"The alkali metal ions lithium, potassium, **rubidium** and cesium depress the rate of spontaneous beating of isolated rabbit right atria. At low concentrations (2 to 4 mM) the negative chronotropic effect was in the order: Cs greater than Rb greater than K or Li; at a higher concentration (12 mM) it was Rb or K greater than Cs or Li. Force of contraction was also depressed by potassium and cesium at all levels, but was stimulated by lithium and by low levels of **rubidium** (2 mM). Lithium had little chronotropic effect up to relatively high concentrations, decreasing spontaneous beating rate to 80% of control at 100 mM LiCl." [rubidium.cesium.lithium.k depress heart rate.doc](#)

"Moreover, the lower concentration of Rb⁺ ions in urine of multiple sclerosis patients, in comparison to healthy individuals and clinical controls as reported previously, was confirmed." [rubidium low in multiple sclerosis.doc](#)

Intraperitoneal administration of lithium (2 mEq/kg/day) was found to increase the superoxide dismutase (SOD) activity in certain brain regions after 24 hours (2 injections) and 3 days (once a day) of exposure. In vitro addition of wide range of lithium (0.1 to 8 mEq) to enzyme preparation as well activated cortical SOD activity; however, at 10 mEq concentrations an inhibition was observed. The increase in SOD activity did

not appear to be region specific as under both in vivo and in vitro conditions lithium enhanced enzyme activity in all the tested brain regions. The effects of intraperitoneal administration of 2 mEq/kg **rubidium** and cesium for 24 hr (2 injections) and 6 days (once a day) were also studied on central SOD. Both the alkali metals were not found to produce any significant alteration in the cortical enzymic activity. When the in vitro effects of these monovalent alkali metals were tested, only 2 mEq **rubidium** was found to increase cortical SOD; however, cesium and potassium at similar concentration did not produce any appreciable effects. It appears from the data that lithium-induced increase in brain SOD activity is not an unspecific effect of alkali metals. SOD enzyme disposes cytotoxic superoxide radicals which, if not removed, could impair the normal functioning of cellular membrane and produce a variety of psychedelic compounds as well. The activation of central SOD by lithium would enhance the disposal process of superoxide radicals whose pathological concentrations may be present in affective disorders. The mechanism of lithium-induced activation of SOD, at present, is not known. [lithium increases SOD.doc](#)

These findings point to a role for lithium and its elemental relatives in the biophysical mechanisms involved with the control of human blood cell production. [lithium.cs.rb important in red cell production.doc](#)

The **rubidium** and lithium ions are known to have opposite effects on a wide range of biochemical and behavioral parameters in experimental animals. Based on the proven effectiveness of lithium as an antimanic agent, several trials have been conducted with **rubidium** in the acute treatment of the depressive phase of bipolar illness. The results to date are promising. However, the 30- to 60-day biologic half-life of **rubidium** has mandated careful studies of potential toxicity before engaging in long-term administration of this ion to depressive subjects. [rubidium.lithium.opposite effects in bipolars.doc](#)

Midbrain raphe lesions in rats (raphe rats) induce aggressive behavior including muricide. A single administration of LiCl (Li) 100 mg/kg to raphe rats produced only 25% of muricide inhibition. However, the inhibitory effect of muricide in raphe rats significantly increased from the 5th day following repeated administration of Li. Chronic Li also inhibited muricide in olfactory bulbectomized (OB) rats. The inhibition of muricide lasted until the next day to some extent. In this point, the effect of Li on muricide is similar to that of antidepressants, but not of neuroleptics. On the contrary, RbCl (Rb) showed a tendency to induce muricide. [rubidium induces muricide in raphe rats.doc](#)

Rubidium (Rb+) has an antidepressive effect and shortens the circadian period in animals, whereas Li+, another alkaline metal, lengthens it. When we treated a depressive Li+ nonresponder with Rb+, we found an improvement of depression as well as a phase advance of the temperature rhythm in relation to the rest-activity rhythm. [rubidium increases antidepressive effect of lithium.doc](#)

The accumulation of 5-HT (after inhibition of monoamine oxidase) and the rate of synthesis of 5-HT in the whole brain (minus cerebellum) were enhanced by dietary and intraperitoneal administration of RbCl, respectively. The effects of lithium and **rubidium**, respectively, on 5HT function in brain are compared. [rubidium effect on 5-HT syndrome.doc](#) A brief overview on the relevance in dietary factors in both development and prevention of cancer is presented. The pharmacologic properties of various food ingredients are discussed. Establishing of a special diet for the cancer patient is suggested. In addition, avoidance of certain foods is recommended to counteract mucus production of cancer cells. Evaluation of the nutrient content of certain diets in regions with low incidence of cancer has advanced the use of certain alkali metals, i.e., **rubidium** and cesium, as chemotherapeutic agents. The rationale for this approach termed the "high pH therapy resides in changing the acidic pH range of the cancer cell by cesium towards weak alkalinity in which the survival of the cancer cell is endangered, and the formation of acidic and toxic materials, normally formed in cancer cells, is neutralized and eliminated. [cesium.rubidium in cancer therapy.doc](#)

These figures are compatible with the hypothesis that the free rubidium or other ions act at the potassium-loading sites at the extracellular face of the pump. [rubidium--ordered release of Rb ions.doc](#)

We studied the effects of permeant ions on the gating of the large conductance Ca(2+)-activated K+ channel from rat skeletal muscle. Rb+ blockade of inward K+ current caused an increase in the open probability as though Rb+ occupancy of the pore interferes with channel closing. In support of this hypothesis, we directly measured the occupancy of the pore by the impermeant ion Cs+ and found that it strongly correlates with its effect on gating. This is consistent with the "foot-in-the-door model of gating, which states that channels cannot close with an ion in the pore. However, because Rb+ and Cs+ not only slow the closing rate (as predicted by the model), but also speed the opening rate, our results are more consistent with a modified version of the model in which the channel can indeed close while occupied, but the occupancy destabilizes the closed state. Increasing the occupancy of the pore by the addition of other permeant (K+ and Tl+) and impermeant (tetraethylammonium) ions did not affect the open probability. To account for this disparity, we used a two-site permeation model in which only one of the sites influenced gating. Occupancy of this "gating site interferes with channel closing and hastens opening. Ions that directly or indirectly increase the occupancy of this site will increase the open probability. [potassium channel gating and blocking by Ca, Rb, Cs.doc](#)

Rubidium concentrations (mmol/l) in male and female controls respectively were: 2.29 +/- 0.29 and 1.96 +/- 0.46 in plasma; 36.79 +/- 5.90 and 30.19 +/- 6.11 in whole blood; 74.57 +/- 10.37 and 72.22 +/- 12.76 in erythrocytes. [rubidium levels higher in males than females.doc](#)

The accumulation of 5-HT (after inhibition of monoamine oxidase) and the rate of synthesis of 5-HT in the whole brain (minus cerebellum) were enhanced by dietary and intraperitoneal administration of RbCl, respectively. [rubidium effects on 5-HT.doc](#)

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SELENIUM

GOOD FOOD SOURCES OF SELENIUM

Selenium content is very dependent upon the content of the soil on which foods and animals are raised.

Brewer's yeast, organ and muscle meats, fish and shellfish, grains, cereals, Brazil nuts, broccoli, cabbage, cucumbers, radishes, garlic, onions, torula yeast, molasses, dairy products, sesame seeds, tuna, kelp, and wheat germ.

This file will get re-written to make it more readable. I will also add footnotes identifying the article and author.

File:

Selenium is essential for the production of glutathione peroxidase (GSHPx or GPX) which is a major detoxifier of chemical toxins, including insecticides, petrochemicals, and other natural and man-made toxic chemicals.

The following study indicates that organophosphorus pesticides both deplete selenium and cause eye damage--perhaps selenium will protect the eyes from TED?

Nippon Ganka Gakkai Zasshi 1996 Jun;100(6):417-32

[Ophthalmopathy due to environmental toxic substances especially intoxication by organophosphorus pesticides].

[Article in Japanese]

Isikawa S.

Department of Ophthalmology, School of Medicine, Kitasato University, Japan.

Organophosphorus pesticides (OPs) produce optico-autonomic peripheral neuropathy in human populations in districts where a large amount of pesticides have been used in agriculture. This report presents an epidemiological study that was performed in Kanagawa Prefecture. An autopsy case of a professional organophosphorus sprayer is reported. In addition, an experiment was performed to investigate a non-cholinergic chronic toxicity due to a certain OP. The epidemiological study revealed that 64 of 7,435 farmers showed vertical smooth pursuit defect of the eyes, impairments of modulation-transfer function (MTF) of the visual system and abnormal contraction dynamics of the pupil reaction to light stimuli, and a high residual level of OP was found in their blood. These abnormalities were reduced by treatment with antidotes such as atropine, prifinium bromide, and pralidoxime methiodide (PAM). The autopsy findings showed severe retinal degeneration with optic neuropathy and an obviously precocious progression of arteriosclerotic change in heart, brain, and retinal vessels. These findings can not be explained by cholinesterase inhibition alone. Experimental evidence showed that OP produced non-cholinergic impairment such as increase of Ca ions in retinal neurons. A generation of free radicals was noted in tissue-cultured retinal neurons. Blood selenium level was reduced by OP. These non-cholinergic actions may also explain the neural damage caused by long-standing low-dosage contact with OPs.

Selenium is an essential component of ID-I which is the enzyme which converts T4 to T3.

Title

The effects of *selenium* deficiency on hepatic type-I iodothyronine deiodinase and protein disulphide-isomerase assessed by activity measurements and affinity labelling.

Author

Arthur JR; Nicol F; Grant E; Beckett GJ

Address

Rowett Research Institute, Bucksburn, Aberdeen, U.K.

Source

Biochem J, 274 (Pt 1):297-300 1991 Feb 15

Abstract

We determined protein disulphide-isomerase (PDI) and iodothyronine deiodinase (ID-I) activities in liver homogenates from rats subjected to *selenium* (Se) and/or iodine deficiencies and food restriction. Additionally, the effects of propylthiouracil (PTU) on the enzymes were studied in vivo and in vitro. *Selenium* deficiency markedly inhibited ID-I activity, but had no significant effects on PDI. Iodine deficiency resulted in a 1.6-fold stimulation in ID-I and a 1.2-fold stimulation in PDI activities. ID-I was much more sensitive than PDI to the inhibitory effects of PTU both in vitro and in vivo. By using a 3,3',5'-tri[125I]iodothyronine affinity label, two major protein bands were identified when hepatic microsomal fractions from Se-sufficient rats were subjected to SDS/PAGE and autoradiography. These bands had molecular masses of 55 and 27.5 kDa, which are similar to those of PDI and ID-I respectively. *Selenium* deficiency resulted in the loss of the 27.5 kDa band, but did not affect the intensity of the 55 kDa band. These results are consistent with the changes in PDI and ID-I enzyme activities. Previous studies have shown that ⁷⁵Se may be incorporated in vivo into the 27.5 kDa protein band. This, taken together with our observation that Se is required for the expression of ID-I and the 27.5 kDa protein band, strongly suggests that ID-I is a selenoprotein.

The following study suggests that selenium deficiency is involved in fibrosis. This proliferation of fibroblasts is also seen in Thyroid Eye Disease, therefore this condition may be a result of

selenium deficiency.

Title

Selenium deficiency and thyroid fibrosis. A key role for macrophages and transforming growth factor beta (TGF-beta).

Author

Contempre B; Le Moine O; Dumont JE; Deneff JF; Many MC

Address

Institute of Interdisciplinary Research (IRIBHN), Free University of Brussels, Medicine Faculty, Belgium.
bcontemp@med.ulb.ac.be

Source

Mol Cell Endocrinol, 124(1-2):7-15 1996 Nov 29

Abstract

Free radical damage and fibrosis caused by *selenium* deficiency are thought to be involved in the pathogenesis of myxoedematous cretinism. So far, no pathway explains the link between *selenium* deficiency and tissue fibrosis. Pharmacological doses of iodine induce necrosis in iodine-deficient thyroids. Necrosis is much increased if the glands are also *selenium*-deficient, which then evolve to fibrosis. This rat model was reproduced to explore the role of *selenium* deficiency in defective tissue repair. At first, proliferation indexes of epithelial cells and fibroblasts were comparable between *selenium*-deficient and control groups. Then, in *selenium*-deficient thyroids the inflammatory reaction was more marked being mainly composed of macrophages. The proliferation index of the epithelial cells decreased, while that of the fibroblasts increased. These thyroids evolved to fibrosis. TGF-beta immunostaining was prominent in the macrophages of *selenium*-deficient rats. Anti TGF-beta antibodies restored the proliferation indexes, and blocked the evolution to fibrosis. In *selenium* deficiency, an active fibrotic process occurs in the thyroid, in which the inflammatory reaction and an excess of TGF-beta play a key role.

Title

[Selenium deficiency and thyroid hormone metabolism and function]

Author

Wu HY; Xia YM; Chen XS

Address

Institute of Nutrition and Food Hygiene, Beijing.

Source

Sheng Li Ko Hsueh Chin Chan, 26(1):12-6 1995 Jan

Abstract

Type I 5'-deiodinase is a Se-containing enzyme. If Se is deficient, the deiodinase activity would be inhibited, the level of circulation T4 will be elevated, and the concentration T3 in peripheral tissues will be decreased. Se deficiency will also accelerate the iodine depletion of thyroid and may even exacerbate some detrimental effects of iodine deficiency. Possibly Se deficiency is involved in the occurrence and development of iodine deficient disorders. *Keshan* disease, with Se deficiency as the major cause, was also observed a change of thyroid hormone metabolism. The change of respiratory enzyme activities in myocardium of *Keshan* disease is in the way somewhat like that of hypothyroidism caused by iodine deficiency. The metabolic change of thyroid hormone after Se deficiency or iodine deficiency may be related to the occurrence of *Keshan* disease.

Title

Mercury/selenium interaction. A comparative study on pigs.

Author

Hansen JC; Kristensen P; Al-Masri SN

Source

Nord Vet Med, 33(2):57-64 1981 Feb

Abstract

A pilot experiment carried out on three pigs have confirmed that interaction between inorganic *mercury* (203HgCl2) and selenium (Na275SeO3) after single intraperitoneal injections are qualitatively uniform in mice and pigs. The detoxifying effect of selenium on *mercury* toxicity seems to be due to a formation of a biologically inactive complex containing the elements in an equimolar ratio. The complex is unable to pass biological barriers, placenta and choroid plexus and is stored in the liver and the spleen.

Title

Improved survival in murine lupus as the result of selenium supplementation.

Author

O'Dell JR; McGivern JP; Kay HD; Klassen LW

Address

Department of Medicine, University of Nebraska Medical Center, Omaha.

Source

Clin Exp Immunol, 73(2):322-7 1988 Aug

Abstract

Selenium is a trace mineral and a required nutrient for animals and humans. Selenium intake appears to be inversely correlated with the risk of developing cancer. Since immunological effects of selenium have been described we studied the capacity of selenium to modify the lupus-like disease of NZB/NZW female mice. Our data indicate that selenium supplementation (sodium selenite 4 parts per million in the drinking water) significantly improves survival in these autoimmune mice: mean survival 55.6 +/- 4.6 weeks (mean +/- s.e.) for treated mice versus 36.1 +/- 1.9 weeks for controls (P less than 0.04). Additionally, selenium supplemented mice had significantly higher natural killer cell activity (P less than 0.001). However, no obvious effects of selenium supplementation on autoantibody production were observed.

Title

[Reference values for blood and serum *selenium* in the Dresden area]

Author

Meissner D

Address

Institut für Klinische Chemie und Laboratoriumsmedizin, Städtisches Klinikum Dresden-Friedrichstadt.

Source

Med Klin, 92 Suppl 30:41-2 1997 Sep 15

Abstract

BACKGROUND: To ensure a correct interpretation of patient's data the regional differences in the supply with *selenium* have to be taken into consideration. **PATIENTS AND RESULTS:** In 256 healthy women and men from the area of Dresden aged 20 to 62 years the *selenium* reference values were examined in blood serum by 1.09 +/- 0.17 (0.75 to 1.43) and in whole blood by 1.29 +/- 0.21 (0.87 to 1.71) mumol/l. There was no dependence upon age and sex and no influence of alcohol, tobacco and vegetarian diet was found. Consumption of beer yeast and frequent fish meals caused improvement of the *selenium* status. **CONCLUSION:** In area of Dresden, similar to the whole of Germany, a marginal *selenium* supply exists. Therefore it is of high importance to consider a balanced nutrition and to control the *selenium* status especially in serious acute diseases and in intensive care.

Title

Selenium regulates gene expression for estrogen *sulfotransferase* and alpha 2U-globulin in rat liver.

Author

Yang Q; Christensen MJ

Address

Department of Food Science and Nutrition, Brigham Young University, Provo, UT 84602, USA.

Source

J Steroid Biochem Mol Biol, 64(5-6):239-44 1998 Mar

Abstract

Dietary intake of the essential trace element selenium (Se) regulates expression of genes for selenoproteins and certain non-Se-containing proteins. However, these proteins do not account for all of Se's biological effects. The objective of this work was to identify additional genes whose expression is regulated by Se. Identification of these genes may reveal new functions for Se or define mechanisms for its biological effects. Weanling male Sprague-Dawley rats were fed a Torula yeast-based Se-deficient basal diet or the same diet supplemented with 0.5 mg Se/kg diet as sodium selenite for 13 weeks. Total RNA was used as template for RNA fingerprinting. Two differentially expressed cDNA fragments were identified and cloned. The first had 99% nucleotide identity with rat liver estrogen *sulfotransferase* (EST) isoform-6. The second had 99% nucleotide sequence identity with rat liver alpha 2u-globulin. The mRNA levels for both were markedly reduced in Se deficiency. Laser densitometry showed that EST mRNA in Se deficiency was 7.3% of that in Se-adequate rat liver. The level of alpha 2u-globulin mRNA in Se-deficient rat liver was only 12.6% of that in Se-adequate rat liver. These results indicate that dietary Se may play a role in steroid hormone metabolism in rat liver.

Med Hypotheses 1993 Aug;41(2):150-9

Selenium—its biological perspectives.

Bedwal RS, Nair N, Sharma MP, Mathur RS

Department of Zoology, University of Rajasthan, Jaipur, India.

Selenium is an essential trace element at lower concentrations and toxic at higher concentration. Animals can metabolize both inorganic and organic forms and convert non methylated Se to mono--or di--or tri--methylated forms, of which, mono-methylated forms are most toxic. Glutathione reductase converts selenogluthathione to H₂S in liver and erythrocytes and is ultimately excreted. Se effects the toxicities of xenobiotic agents, provides antagonistic effect to Sulphur and co-administration with Zn increase Se retention in certain organs. At its toxic level (4-8 ppm) it increases Cu contents of heart, liver and kidney and has detoxifying or protecting effect against Cd and Hg. It is a prosthetic group of several seleno metalloenzymes. The concentration of the element is decreased in serum/plasma or erythrocytes of patients of AIDS, trisomy-21, Crohn's and Down's syndrome, phenylketonurea, Keshan's disease and cancer. Rather, the element has antiproliferative and cancer protecting effect. Se content of testes increases considerably during pubertal maturation and, during Se deficiency, the supply to the testes has priority over the other tissues. The element is localized in the mitochondrial capsule protein (MCP) and is involved in biosynthesis of testosterone. Neither the age of mother nor the concentration of Se during pregnancy has any effect on weight of baby or the length of pregnancy. Se levels in human milk is affected by maternal intake and its requirements by infants and young children are higher for their rapid growth. Clinical symptoms of its toxicity include severe

irritations of respiratory system, metallic taste in mouth, formication of nose, signs of rhinitis, lung edema and broncho-pneumonia. The typical garlic odour of breath and sweat is due to dimethyl-selenide.

Publication Types:

Cadmium is the strongest selenium antagonist.

Title

Amounts of twelve elements required to induce selenium-vitamin E deficiency in ducklings.

Author

Van Vleet JF

Source

Am J Vet Res, 43(5):851-7 1982 May

Abstract

Mortality and myopathy of selenium-vitamin E (Se-E) deficiency was produced, in a concentration-dependent pattern, during a 4-week study of 750 ducklings fed a commercial duck starter mash that contained adequate amounts of Se and E, and supplemented with multiple amounts of Ag (50 to 3,000 mg/kg of feed, as acetate), Zn (3,000 to 6,000 mg/kg, as sulfate), Cd (10 to 500 mg/kg, as sulfate), Te (25-500 mg/kg, as tetrachloride), Co (100 to 1,000 mg/kg, as chloride), Cu (500 to 1,500 mg/kg, as sulfate), Hg (200 to 400 mg/kg, as chloride), and Sn (1,000 mg/kg, as chloride). Also, feeding supplements of Pb (500 mg/kg, as acetate), As (600 mg/kg, as sodium arsenilate), Fe (5,000 mg/kg, as sulfate), and S (5,000 mg/kg, as sodium sulfite) produced a low-to-medium frequency of lesions of Se-E deficiency. In ducklings with muscle lesions, the gizzard was most often affected (84.2%), followed in decreasing order by skeletal muscles (69.7%), intestine (34.9%), and heart (23.0%). The frequency of skeletal muscle lesions was high in birds fed Ag, and myocardial necrosis was frequent in ducklings fed Te and Hg. Ducklings affected with myopathy were reluctant to stand. Subcutaneous edema, with or without hemorrhages, and pale areas of myonecrosis in gizzard, skeletal muscles, intestine, and heart were seen at necropsy. Birds fed Te and Hg often had hydropericardium and hemorrhagic myocardial necrosis. Seemingly, addition of many elements to a Se-E adequate commercial diet will increase the requirement for Se-E. In our duckling model, minimal amounts shown to induce Se-E deficiency were 50 mg of Ag/kg, 3,000 mg of Zn/kg, 10 mg of Cd/kg, 25 mg of Te/kg, 1200 mg of Co/kg, 500 mg of Cu/kg, 200 mg of Hg/kg, 1,000 mg of Sn/kg, 500 mg of Pb/kg, 600 mg of As/kg, 5,000 mg of Fe/kg, and 5,000 mg of S/kg.

Altern Ther Health Med 1996 Jul;2(4):59-62, 65-7

Published erratum appears in *Altern Ther Health Med* 1996 Sep;2(5):101

Selenium: a quest for better understanding.

Badmaev V, Majeed M, Passwater RA

Sabinsa Corporation, Piscataway, NJ, USA.

Selenium is an essential trace element in nutrition for the prevention of disease in humans. Epidemiological studies indicate an association between low nutritional selenium status and increased risks of cardiomyopathy, cardiovascular disease, and carcinogenesis in various sites of the body. The role of selenium supplementation in the prevention and treatment of AIDS-related pathology has been considered. Selenoproteins discovered in mammalian cells may account for the essentiality of selenium in the body's antioxidant defense; thyroid hormone function; immune system function, particularly the cellular immunity; formation of sperm; and functioning of the prostate gland. The seleno-organic compounds, primarily L-(+)-selenomethionine, generally are recognized as safe and effective forms of selenium supplementation. The nutritionally recommended dose of elemental selenium is estimated at 50 to 200 micrograms [corrected] per day. There is, however, increased discussion of a pharmacological dose of selenium, significantly higher than the nutritional dose of the microelement, to treat active conditions. One way of increasing the tissue levels of selenium is to combine its ingestible form with a nutrient bioavailability enhancing compound.

Selenium is essential for the production of testosterone. Since selenium and vitamin E work together, this is probably the reason that vitamin E is recommended for male sex hormone production.

J Reprod Fertil 1996 Mar;106(2):291-7

Effects of selenium deficiency on testicular morphology and function in rats.

Behne D, Weiler H, Kyriakopoulos A.

Department 'Trace Elements in Health and Nutrition', Hahn-Meitner-Institut Berlin, Germany.

For four generations rats were fed a low selenium diet (2-7 micrograms Se kg⁻¹) or the same diet with 250 or 300 micrograms Se kg⁻¹ added as selenite. In male rats of the first generation that had been fed the diets from the age of 20 days onwards, selenium depletion led to slightly delayed testis growth during pubertal development that was compensated for in the later stages of maturation. In adult rats fed the low selenium diet for nearly a year no changes in testicular mass and morphology were observed. The serum concentration of testosterone of 6-month-old, selenium-depleted animals was, however, slightly lower than that of adequately supplied controls, and the stimulation of testosterone secretion by administration of GnRH or LH resulted in a significantly less marked rise in the serum concentration of testosterone. From the second generation onwards

the testis mass, expressed as a percentage of the body mass, decreased and in the fourth generation was less than 50% of that of the controls. The male gonads of fourth generation animals showed a severe bilateral atrophy, in which the seminiferous tubules were considerably reduced in diameter and almost entirely lined by Sertoli cells and a few stem cells. Differentiated spermatozoa could not be detected. The alterations were reversible and spermatogenesis was restored by feeding the selenium-adequate diet. The findings indicate that testicular morphology and functions are affected by severe selenium deficiency and that the element is necessary for testosterone biosynthesis and the formation and normal development of spermatozoa.

Selenium deficiency in childhood may predispose persons to multiple sclerosis. [..America Online 4.0/download/multiple sclerosis--childhood def.of selenium.doc](#)

Low T3/T4 ratio is due to a selenium deficiency. [..America Online 4.0/download/low t3-t4 ratio.txt](#)

The following study shows that low selenium levels are associated with greatly increased risk for thyroid cancer.

Title

Prediagnostic serum selenium in a case-control study of thyroid cancer.

Author

Glattre E; Thomassen Y; Thoresen SO; Haldorsen T; Lund-Larsen PG; Theodorsen L; Aaseth J

Address

Cancer Registry of Norway, Oslo.

Source

Int J Epidemiol, 18(1):45-9 1989 Mar

Abstract

Sera from 43 persons who developed thyroid cancer on an average 4.8 years after blood sampling were compared with sera from controls. Three controls per case matched for sex, age, place of residence and year of blood sampling, with regard to serum selenium and serum *copper*. Cases were significantly lower in serum selenium than controls, and the estimated odds ratio of thyroid cancer increased from 1 for levels greater than or equal to 1.65 mumol/l, to 6.1 for levels 1.26-1.64 mumol/l, to 7.7 for levels less than or equal to 1.25 mumol/l. When time from blood sampling to diagnosis of the case was considered, it could be shown that the protective effect of high serum selenium concentrations was restricted to the last (less than 7) years prior to the diagnosis of thyroid cancer. The serum selenium concentration of cases tended to decrease relative to controls the shorter time was from blood sampling to the diagnosis. There was no difference between cases and controls with regard to serum *copper*.

Interaction of selenium, zinc, and iodine effects on the thyroid. [..America Online 4.0/download/selen.zn.iodine deficiency effects on thyroid 4.12.99.txt\](#)

A good question is, does high intake of selenium lead to high deiodinase enzyme activity and thus high levels of T3 and hyperthyroidism. A study showed that excessive amounts of selenium does not lead to higher D-I activity.

Title

Type I iodothyronine deiodinase activity after high selenium intake, and relations between selenium and iodine metabolism in rats.

Author

Behne D; Kyriakopoulos A; Gessner H; Walzog B; Meinhold H

Address

Hahn-Meitner-Institut Berlin, Germany.

Source

J Nutr, 122(7):1542-6 1992 Jul

Abstract

Type I iodothyronine deiodinase (I-D), which catalyzes the production of the thyroid hormone 3,3',5-triiodothyronine from thyroxine, has recently been identified as a selenoenzyme. It is therefore of interest to investigate the relationships between selenium and iodine metabolism. In the livers of Se-deficient rats I-D activity was inhibited; the production of 3,3',5-triiodothyronine and 3,3'-*diiodothyronine* from added thyroxine was decreased by greater than 95% relative to Se-adequate controls. The hepatic I-D activity was also reduced in rats fed a diet with a low iodine concentration. Unaltered glutathione peroxidase activities in liver and plasma of these rats suggest, however, that with normal Se intake this metabolic pathway of Se is not affected by iodine depletion. When rats were administered ⁷⁵Se-labeled selenium at levels equal to the amounts ingested from diets with Se concentrations of 0.3 or 2 mg Se/kg, greater Se concentrations were found in the thyroid and liver of the animals receiving the higher dosage. The thyroidal 3,3',5-triiodothyronine and thyroxine concentrations, however, were comparable in rats fed diets with 0.3 mg Se/kg diet as selenite and 2 mg Se/kg as selenite or L-selenomethionine. The measurement of the hepatic I-D and glutathione peroxidase activities in these animals showed that excessive Se supply does not elevate the activities of the two enzymes but might even have the opposite effect. At high Se intake tissue Se concentration cannot therefore be used as indicator of the selenoenzyme activities.

Selenium may be involved in the etiology of osteoarthritis. "The pathophysiology of secondary osteoarthritis remains largely obscure. Our attention has been drawn to Kashin-Beck disease (KBD), which has been attributed to Se deficiency." [selenium deficiency in etiology of osteoarthritis.doc](#)

Selenium sources: beer. A study of trace minerals in beverages in France showed that selenium is provided by beer: "Alcoholic drinks represent 35% of the daily intake of beverages; they are likewise the main source of minerals such as: iodine and iron (wine), *selenium* (beer), fluorine, calcium and copper (in all alcoholic drinks)."

A study of selenium in Germany showed that the soils in Germany are very low in selenium and the largest contributions to selenium in the German diet come from beer and seafood. This may explain the high incidence of thyroid disease in Germany and the high intake of beer there. "Consumption of beer yeast and frequent fish meals caused improvement of the *selenium* status. CONCLUSION: In area of Dresden, similar to the whole of Germany, a marginal *selenium* supply exists. Therefore it is of high importance to consider a balanced nutrition and to control the *selenium* status especially in serious acute diseases and in intensive care." [selenium sources in germany--beer and seafood.doc](#)

"Selenium - sources of the antioxidant selenium are brazil nuts, brewers yeast, kelp, brown rice, liver, molasses, seafood, wheatgerm, whole-grains, garlic and onions." [liver health--Dr. Sandra Cabot.doc](#)

"The effectiveness of a peroral *sodium* selenite therapy (115 micrograms Se/m² BSA/d) administered to cystic fibrosis patients (n = 32) could after three months be identified in a significant serum selenium increase (0.69-->0.96 mumol/L), a significant malondialdehyde decrease (2.72-->1.64 mumol/L), as well as in a significant serum vitamin E increase (4.31-->5.72 micrograms/mL). Parallel to that, a serum T3 increase as well as a highly significant decrease in the serum T4/T3-ratio were found, too, which point to improved peripheral T4-->T3 conversion during selenium medication." [selenium improves cystic fibrosis and increases T3.doc](#)

The effects of sublethal doses of selenite, selenate, selenocystine (Se-Cys) and selenomethionine (Se-Met) as well as of tellurite on body temperature and feeding behavior were examined in male ICR mice. Ten or 30 mumol/kg of chemicals were injected subcutaneously and body temperature was measured up to 4 h. In a separate experiment, the gastric content was weighted 4 h after injection. All chemicals except Se-Met induced both hypothermia and hyperphagia, suggesting that: (a) these two effects are related to each other; (b) among the chemicals tested, Se-Cys appears to be the most potent hypothermia inducer; (c) Se-Met is unique in that it has neither effect. [selenium cysteine and methionine effects on hypothermia.doc](#)

"Seemingly, addition of many elements to a Se-E adequate commercial diet will increase the requirement for Se-E. In our duckling model, minimal amounts shown to induce Se-E deficiency were 50 mg of Ag/kg, 3,000 mg of Zn/kg, 10 mg of Cd/kg, 25 mg of Te/kg, 1200 mg of Co/kg, 500 mg of Cu/kg, 200 mg of Hg/kg, 1,000 mg of Sn/kg, 500 mg of Pb/kg, 600 mg of As/kg, 5,000 mg of Fe/kg, and 5,000 mg of S/kg." [selenium--amounts of 12 elements to produce deficiency.doc](#)

In the low-Se group, impaired weight gain was observed from the 5th mo, and head alopecia was found in 60% of the animals. Microscopically, no clear changes in the articular chondrocytes were apparent, whereas with the electron microscope, chondrocytes in the deep layer showed degeneration of nuclei and endoplasmic reticular ballooning. [selenium deficiency alopecia.articular cartilage.doc](#)

OBJECTIVE: To study the relationships between fish intake and different markers of selenium status and thyroid hormone function. DESIGN: Cross-sectional study. SETTING AND SUBJECTS: Sixty-eight men (age 24-79 years) were recruited among coastal fishermen and inland subjects from Latvia. None of the subjects was on selenium medication or had any known endocrine disease. MAIN OUTCOME MEASURES: Correlations between fish intake, plasma levels of selenium, selenoprotein P, glutathione peroxidase, organic mercury in erythrocytes and TSH in serum. RESULTS: Selenium in plasma ranged from 0.30 to 1.56 micromol/l, selenoprotein P from 0.54 to 2.21 arbitrary units relative to pooled plasma, and glutathione peroxidase from 1.20 to 5.73 mg/l. The number of fish meals per month was correlated with plasma selenium, selenoprotein P and glutathione peroxidase (r = 0.63, r = 0.62 and r = 0.50, respectively; P < 0.001). Plasma selenium was correlated with selenoprotein P and glutathione peroxidase (r = 0.88 and r = 0.67, respectively; P < 0.001), and also selenoprotein P and glutathione peroxidase were correlated (r = 0.63, P < 0.001). The mean plasma selenium level in those with a high fish intake (21-50 fish meals/month), was 81% higher than in those with lowest fish intake. TSH in serum was inversely correlated with plasma selenium and selenoprotein P. Thyroid hormone levels were not correlated with plasma selenium, selenoproteins or fish intake. CONCLUSIONS: In this study group, selenium from fish intake had a marked impact on all variables studied on selenium status. No impact of selenium status on T3 and T4 levels was observed. The slightly negative correlation of selenium status with TSH levels might indicate a higher TSH secretion at low selenium status. [selenium levels in fish eaters does not affect T4 or T3 levels.doc](#)

Selenium is a trace mineral and a required nutrient for animals and humans. Selenium intake appears to be inversely correlated with the risk of developing cancer. Since immunological effects of selenium have been described we studied the capacity of selenium to modify the lupus-like disease of NZB/NZW female mice. Our data indicate that selenium supplementation (sodium selenite 4 parts per million in the drinking water) significantly improves survival in these autoimmune mice: mean survival 55.6 +/- 4.6 weeks (mean +/- s.e.) for treated mice versus 36.1 +/- 1.9 weeks for controls (P less than 0.04). Additionally, selenium supplemented mice had significantly higher natural killer cell activity (P less than 0.001). However, no obvious effects of selenium supplementation on autoantibody production were observed. [selenium increases survival in autoimmune diseased mice.doc](#)

Apart from the essential trace element iodine, which is the central constituent of thyroid hormones, a second essential trace element, selenium, is required for appropriate thyroid hormone synthesis, activation and metabolism. The human thyroid gland has the highest selenium content per gram of tissue among all organs. Several selenocysteine-containing proteins respectively enzymes are functionally expressed in the thyroid, mainly in thyrocytes themselves: three forms of glutathione peroxidases (cGPx, pGPx, and PH-GPx), the type I 5-deiodinase, thioredoxin reductase and selenoprotein P. The thyroidal expression of type II 5-deiodinase still is controversial. As thyrocytes produce H₂O₂ continuously throughout life an effective cell defense system against H₂O₂ and reactive oxygen intermediates derived thereof is essential for maintenance of normal thyroid function and protection of the gland. In experimental animal models long-term and strong selenium deficiency leads to necrosis and fibrosis after high iodide loads. Combined iodide and selenium deficiency such as in central Zaire is thought to cause the myxedematous form of endemic cretinism. Inadequate selenium supply and prediagnostically low serum selenium levels are significantly correlated with the development of thyroid carcinoma and other tumors. Though selenium supply controls expression and translation of selenocysteine-containing proteins no direct correlation is found between selenium tissue content and expression of various thyroidal selenoproteins, indicating that other regulatory factors contribute to or override selenium-dependent expression control, e.g., in thyroid adenoma, carcinoma or autoimmune disease. As both trace elements, iodine and selenium, were washed out from the upper layers of the soil during and after the ice ages in many regions of the world adequate supply with these essential compounds needs to be provided either by a balanced diet or supplementation. [selenium and the thyroid gland.doc](#)

Selenium is an essential trace element in nutrition for the prevention of disease in humans. Epidemiological studies indicate an association between low nutritional selenium status and increased risks of cardiomyopathy, cardiovascular disease, and carcinogenesis in various sites of the body. The role of selenium supplementation in the prevention and treatment of AIDS-related pathology has been considered. Selenoproteins discovered in mammalian cells may account for the essentiality of selenium in the body's antioxidant defense; thyroid hormone function;

immune system function, particularly the cellular immunity; formation of sperm; and functioning of the prostate gland. The seleno-organic compounds, primarily L-(+)-selenomethionine, generally are recognized as safe and effective forms of selenium supplementation. The nutritionally recommended dose of elemental selenium is estimated at 50 to 200 micrograms [corrected] per day. There is, however, increased discussion of a pharmacological dose of selenium, significantly higher than the nutritional dose of the microelement, to treat active conditions. One way of increasing the tissue levels of selenium is to combine its ingestible form with a nutrient bioavailability enhancing compound.[selenium--essentiality in thyroid function.doc](#)

Mercury (Hg) and selenium (Se) concentrations were determined by radiochemical neutron activation analysis in samples from the pituitary glands, occipital cortices, renal cortices, abdominal muscles, and thyroid glands of cadavers. Samples were retrieved from dental staff occupationally exposed to Hg and from the general population. Increased concentrations of both Hg and Se in samples from dental staff showed that Se accumulated together with Hg. Regression analysis of data from the pituitary glands and occipital cortices of dental staff indicated the accumulation of Se at a rough stoichiometric ratio of 1:1 with Hg. The same stoichiometric ratio between the elements was seen in the renal cortices from the general population. The regression analysis showed that a substantial fraction of Se was not associated with Hg; it is assumed that this corresponds to biologically available Se. Concentrations of biologically available Se decreased with advancing age in the pituitary gland, but not in other organs, and varied appreciably between organs.[mercury and selenium concentrations in dental staff.doc](#)

The prevalence of abnormalities and associated tissue selenium residues were assessed for the fish population of Belews Lake, North Carolina, and two reference lakes in 1975, 1978, 1982, and 1992. Teratogenic defects identified included lordosis, kyphosis, scoliosis, and head, mouth, and fin deformities. Many fish exhibited multiple malformations and some were grossly deformed and distorted in appearance. Other abnormalities observed were edema, exophthalmus, and cataracts. Whole-body tissue residues of selenium in the fishes of Belews Lake were up to 130 times those in the reference lakes and the incidence of abnormalities was some 7 to 70 times greater. Teratogenic defects increased as selenium levels rose between 1975 and 1982 and fell with declining selenium levels between 1982 and 1992 as selenium inputs into Belews Lake were curtailed. The relationship between selenium residues and prevalence of malformations approximated an exponential function ($R^2 = 0.881$, $P < 0.01$; cubic model) for centrarchids over the range of 1-80 micrograms/g dry wt selenium and 0-70% deformities. This relationship could be useful in evaluating the role of teratogenic effects in warm-water fish populations suspected of having selenium-related reproductive failure. Unique conditions may have existed in Belews Lake which led to the high frequency and persistence of deformities in juvenile and adult fish. In other, less-contaminated locations competition and predation may eliminate malformed individuals in all but the larval life stage. Teratogenesis could be an important, but easily overlooked phenomenon contributing to fishery reproductive failure in selenium-contaminated aquatic habitats.[selenium toxicity effects in freshwater fish.doc](#)

Growth rate of Single Combe White Leghorn cockerels fed a casein-gelatin-glucose diet was significantly depressed at two weeks when 10 p.p.m. or more selenium was added to the diet. When 20% *linseed* meal was included in the diet, growth was not reduced with 10 p.p.m. selenium and only slightly reduced with 20 p.p.m. selenium. Including 20% soybean meal failed to modify the toxicity. Levels of 5 and 10% *linseed* meal were less effective in counteracting selenosis than was 20%. Fractionation studies showed that a protective factor in *linseed* meal was extracted by methanol and ethanol and was not destroyed by autoclaving. Ashing the ethanol extract destroyed its activity. The factor was readily extracted by chloroform:methanol (2:1) but less effectively by acetone and diethyl ether. Washed chloroform:methanol extract was inactive but the washings contained the factor. Concentrates of the factor were active at less than 1% of the dry matter of the diet. The results of these studies show that *linseed* meal contains a heat stable, organic, polar factor that modified selenium toxicity in the chick.[flaxseed modifies selenium toxicity.doc](#)

Selenium is an essential trace element at lower concentrations and toxic at higher concentration. Animals can metabolize both inorganic and organic forms and convert non methylated Se to mono- or di- or tri-methylated forms, of which, mono-methylated forms are most toxic. Glutathione reductase converts selenogluthathione to H₂S in liver and erythrocytes and is ultimately excreted. Se effects the toxicities of xenobiotic agents, **provides antagonistic effect to Sulphur and co-administration with Zn increase Se retention in certain organs**. At its toxic level (4-8 ppm) it increases Cu contents of heart, liver and kidney and has **detoxifying or protecting effect against Cd and Hg**. It is a prosthetic group of several seleno metalloenzymes. The concentration of the element is decreased in serum/plasma or erythrocytes of patients of AIDS, trisomy-21, Crohn's and Down's syndrome, phenylketonurea, Keshan's disease and cancer. Rather, the element has antiproliferative and cancer protecting effect. Se content of testes increases considerably during pubertal maturation and, during Se deficiency, the supply to the testes has priority over the other tissues. The element is localized in the mitochondrial capsule protein (MCP) and is involved in biosynthesis of testosterone. Neither the age of mother nor the concentration of Se during pregnancy has any effect on weight of baby or the length of pregnancy. Se levels in human milk is affected by maternal intake and its requirements by infants and young children are higher for their rapid growth. Clinical symptoms of its toxicity include severe irritations of respiratory system, metallic taste in mouth, formication of nose, signs of rhinitis, lung edema and broncho-pneumonia. **The typical garlic odour of breath and sweat is due to dimethyl-selenide.**[selenium--biologic effects and toxicity.doc](#)

Nutrition Almanac, pg. 133 (Selenium): "Overdoses (of selenium) can interfere with fluoride assimilation, which helps prevent tooth decay. Children who live in areas where the soil is rich in selenium show signs of increased decayed, missing and filled teeth."

The following study indicates that taking vitamin C in gram quantities can interfere with selenium absorption.

N Z Med J 1985 Aug 14;98(784):627-9

Effect of a megadose of ascorbic acid, a meal and orange juice on the absorption of selenium as sodium selenite.

Robinson MF, Thomson CD, Huemmer PK

Urinary and faecal excretions of selenium were measured for five days following a dose of 1 mg Se as sodium selenite in ten young women after an overnight fast. The selenite was taken two hours before a meal or mixed with 1 g ascorbic acid; or with a continental type breakfast providing 4.5-5.6 micrograms Se and 0.6-0.8 mg Cu, with or without 200 ml orange juice (60 mg ascorbic acid). The light meal appeared to have little effect on selenite-Se absorption, and orange juice appeared even to assist it. **But the availability of Se was reduced almost to zero when selenite and 1 g ascorbic acid were taken together well before the meal.**

PMID: 3861972, UI: 85297084

Interactions between selenium and iodine

April 27, 1999

Selenium and iodine are two minerals which are critically important in the proper functioning of the thyroid. While the importance of iodine has been known a long time, the importance of selenium has only been discovered and explored since 1990. Much research is presently being conducted on the functions of these two minerals in thyroid function and it is becoming clear that there is an interaction between the two. Iodine has a seemingly simple role in the thyroid-it is incorporated into the thyroid hormone molecule.

A deficiency of iodine will cause hypothyroidism and if this is severe and occurs during pregnancy, the offspring will be mentally damaged and

is called a cretin. Cretinism, or myxedematous cretinism as it is sometimes called, is not only caused by an iodine deficiency, but is also influenced by a selenium deficiency. Iodine apparently has just one function in the body—in the thyroid.

Selenium, on the other hand, performs many functions. At the beginning of the 1990s it was discovered that the deiodinase enzymes which convert T₄ (thyroxine, the thyroid prohormone) into T₃ (triiodothyronine, the cellularly active hormone) and also convert T₃ into T₂, thereby degrading it, are selenium enzymes (formed with the amino acid cysteine). This discovery has led to a lot of research studies on the effects of selenium, iodine, and their interactions.

Selenium also performs other important roles in the body. The most important of these is probably as its role as the body's best antioxidant (anti-peroxidant). It performs this role as part of glutathione peroxidase (GSHPx or GPX). As part of GPX, selenium prevents lipids and fats from being peroxidized (oxidized), which literally means that it prevents fats from going rancid (this can be seen on your skin as "age spots" or "liver spots" (autopsies show that skin "liver spots" are accompanied by similar spots of peroxidized fats in the liver.) Therefore selenium protects all of the cellular membranes, which are made up of fats, from peroxidation. Peroxidation of cellular membranes reduces the ability of the membrane to pass nutrients including minerals and vitamins, so selenium deficiency is the first step toward developing the many problems caused by nutrient deficiencies.

Joel Wallach considers a selenium deficiency combined with high intake of vegetable oils (salad dressings, margarine, cooking oils) as the "quickest route to a heart attack and cancer." It seems that the body uses a lot of selenium to protect the fats from peroxidation. Polyunsaturated fats which are hydrogenated or heated become the same as rancid fats and large amounts of selenium are then needed to protect the body. Consumption of these dietary fats can thus lead to a selenium deficiency.

Selenium is also essential for the production of estrogen sulfotransferase which is the enzyme which breaks down estrogen. A deficiency of selenium can thus lead to excessive amounts of estrogen, which may depress thyroid function, and also upset the progesterone-estrogen balance.

Wallach also lists other effects of selenium deficiency: anemia (red blood cell fragility), fatigue, muscular weakness, myalgia (muscle pain), muscular dystrophy (white muscle disease in animals), cardiomyopathy (sudden death in athletes), heart palpitations, irregular heartbeat, liver cirrhosis, pancreatitis, Lou Gehrig's and Parkinson's diseases (mercury toxicity), Alzheimer's Disease (high intake of vegetable oil), sudden infant death syndrome (and possibly "breathlessness" in adults, j), cancer, multiple sclerosis, and sickle cell anemia.

Selenium is essential for the production of testosterone. A deficiency seems to be involved in osteoarthritis. I've found studies linking selenium deficiency to alopecia (hair loss) and to degeneration of the knee joint (seen in Kashin-Beck disease). Since selenium is necessary to produce GPX which is a major detoxifier of man-made and environmental toxins, selenium deficiency can lead to chemical and drug sensitivities.

These are some of the non-thyroidal effects of selenium deficiency. The effects of selenium deficiency on thyroidal health is even more interesting. One study I read indicated that in experimental animals, selenium deficiency will increase T₃ in the heart. This may be the reason that selenium deficiency causes heart palpitations and rapid heart beat, which is common in thyroid disease.

While we've seen that selenium deficiency will interfere with T₄ to T₃ conversion and lead to functional hypothyroidism (low T₃ phenomenon), selenium plays another vital role in the thyroid as part of GPX. During the production of thyroid hormone, hydrogen peroxide (H₂O₂) is produced. H₂O₂ is important for the production of thyroid hormone, but excessive amounts lead to high production of thyroxine (T₄) and also damage to the cells of the thyroid. GPX plays the extremely vital role of degrading H₂O₂ and thereby limiting hormone production and preventing damage to the thyroid cells. This seems to be the main way in which selenium protects the thyroid from sustaining damage which can lead ultimately to cancer.

Without selenium, the thyroid gland becomes damaged and it is through this mechanism that the main selenium and iodine interactions are found. An iodine deficiency will cause goiter, an enlargement of the thyroid gland produced by the body in an attempt to increase hormone production from limited amount of iodine. Selenium deficiency increases the weight of the thyroid in experimental animals, and a selenium deficiency combined with an iodine deficiency leads to a further increase in thyroidal weight (bigger goiter). In African countries like Zaire, there are areas where both iodine and selenium are very scarce in the soil (these deficiencies seem to run parallel in most areas). Consequently a high percentage of the people have goiters and hypothyroidism. An experimental attempt was made to correct the selenium deficiency and the result was that the hypothyroidism was made WORSE in the hypos and it produced hypothyroidism in some euthyroid subjects. This was entirely unexpected and the experimenters issued a warning about supplementing with selenium (and not iodine) when both deficiencies exist concurrently.

The body has a compensatory mechanism to maintain T₃ levels when iodine is deficient—it increases the production of the deiodinase Type I enzyme (DI-I). This is not a small increase, but has been shown in cattle to be an increase of 10-12 times. This increase in DI-I increases the conversion of the existing T₄ to T₃ to maintain T₃ levels, but also increases the conversion of T₃ to T₂ (the degraded by-product of T₃). Because of the iodine deficiency, T₄ is not replenished and T₃ ultimately decreases from the lack of sufficient T₄ leading to a worsening of the hypothyroidism.

This result is made worse by another phenomenon which hasn't been thoroughly studied: a selenium deficiency causes an iodine deficiency to get worse. This may be a protective adaptation by the body to limit the damage caused to the thyroid when selenium is deficient and iodine is adequate. Let's examine this part of the interaction.

We've all heard that many doctors tell hypo patients, especially those with Hashimoto's thyroiditis, not to take iodine because it can aggravate their condition. The reason seems to be that selenium protects the thyroid gland from oxidative damage and this damage can increase significantly if iodine is supplemented. Taking iodine will increase thyroid hormone production and the production of H₂O₂ which damages the thyroidal cells. The lack of selenium prevents GPX from being able to protect the cells from this oxidative damage. While I doubt if most doctors realize why iodine should be restricted (it certainly seemed counter-intuitive to me at first), they have learned through experience that iodine can increase the thyroid damage in Hashimoto's. The information that selenium should be supplemented along with iodine is so new that most of them are unaware of it.

Here's what we have: Studies have shown that if iodine is low, selenium must also be kept low to prevent the hypothyroidism from becoming worse (from increased DI-I and T₄ depletion, as explained above.) So if both minerals are low, then the person is hypo and gets a goiter, but the damage to the thyroid is kept to a minimum. More severe problems happen when either selenium or iodine is high and the other is low. If selenium is high and iodine low, then T₄ to T₃ to T₂ conversion is accelerated without T₄ being replenished, leading to a worsening of the hypoT. If iodine is high and selenium is low, then H₂O₂ is not degraded by GPX. Since H₂O₂ drives the thyroid hormone production, then the thyroid over-produces thyroid hormone (Grave's hyperthyroidism), the thyroid is damaged from the oxidation by the H₂O₂, and the end result is that the damaged thyroid ultimately decreases activity and hypothyroidism results (Hashimoto's thyroiditis). This could explain the observed progression of Grave's to Hashimoto's.

If a selenium deficiency causes an iodine deficiency, leaving you both selenium and iodine deficient, and supplementing with either selenium or iodine causes severe problems, then the only solution is to supplement both selenium and iodine simultaneously and gradually. Even then you could experience an immediate boost (from increased conversion of T₄ to T₃) with a subsequent letdown (lack of T₄ production because of insufficient iodine or other necessary nutrient). You have to be prepared to ride out the tough times and continue increasing the selenium and iodine until those two deficiencies are corrected and the respective metabolic pathways are back working properly.

Everything that I've read about selenium indicates that it is absolutely essential for proper functioning of the thyroid. A deficiency of selenium

may lead to either hyperthyroidism or hypothyroidism. I've always wondered if high intake of selenium can lead to hyperthyroidism and finally found someone who did the experiment. They found that a high intake of selenium will not increase T4 production and lead to hyperthyroidism.

If a person has hyperT, then it looks like taking selenium without iodine will result in a decrease in production of T4 (although there may be an initial transient increase in T4 to T3 conversion and hence higher T3). I would suggest to start with a small amount of selenium methionine (about 50 mcg) and gradually increase it. I cannot see any way that thyroid function can be normalized without selenium.

For hypos the important message is that a selenium deficiency may cause an iodine deficiency, so that even though you are taking iodine you may not be assimilating it unless selenium is also being taken. This would explain how people can have iodine deficiencies even though salt and many foods have iodine added. Supplement with both iodine and selenium. I would recommend starting with 100 mcg of selenium and one kelp tablet and gradually work up to 400-600 mcg of selenium and 2-4 tablets of kelp.

While I've found research on the interactions of iodine and selenium, there are two other minerals which need to be studied for their interactions with these two: zinc and copper. I found one study which examined the complex interactions of selenium, iodine, and zinc (there are interactions), but none which have looked at all four minerals in a 4 X 4 factorial design. Now that would be an interesting study! Hopefully someone will do that soon.

I think one lesson from studying the interactions of selenium and iodine is that the interrelationships between minerals are very complicated. Supplementing with one or two can cause further problems. You have to make sure that you correct every deficiency. Health is built from a chain of nutrients and, like a chain, health cannot be accomplished if one nutrient is missing. Sometimes it's complicated putting the chain back together without running into problems (like supplementing with either selenium or iodine, but not both), but every deficiency has to be corrected. John

Experimental data linking the connection between mineral deficiencies and malfunctions of the immune system are rare. In the copper file, there are studies indicating that copper deficiency is involved in immune system dysfunction. The following article offers some evidence that a selenium deficiency is also involved in the malfunction of the immune system in autoimmune diseases such as thyroid disease. This article is reprinted from Mary Shomon's site at About.com.

Special to DG News

DENVER, CO -- June 22, 2001 -- Selenium supplementation may prevent progression of autoimmune thyroid disease, especially during the onset of the disease, according to researchers.

Dr. Barbara Gasnier with the Medizinische Klinik University, Munich, Germany, reported the findings today at the 83rd Annual Meeting of the Endocrine Society (ENDO) in Denver, Colorado.

According to the researchers, selenium deficiency may contribute to the development and maintenance of autoimmune thyroiditis because of its effect on the function of selenium-dependent enzymes, which can modulate the immune system.

Dr. Gasnier and her colleagues performed a blinded, placebo-controlled, prospective study in 72 women with autoimmune thyroiditis, average age 42, with thyroid peroxidase antibodies and/or thyroglobulin antibody levels greater than 350 U/mL.

Patients were randomized into two groups matched in aged and antibody levels. A total of 36 patients received 200 mcg of sodium selenite per day for three months, and 36 patients received placebo. All patients were substituted with L-thyroxine to maintain thyrotrophin (TSH) levels within the normal range.

The researchers then measured the change in the autoantibody concentration as a marker for the activity of the disease.

After three months, nine patients in the selenium treated group had completely normalized antibody titers in contrast to only two patients in the placebo group. In addition, the mean thyroid peroxidase antibody concentrations decreased significantly to 51 percent in the selenium group compared to 90 percent in the placebo group. The thyroglobulin antibodies concentrations, a marker of humoral immunity, were unchanged in both groups, however.

The effect was more pronounced in patients with high thyroid peroxidase antibody concentrations. An analysis of eight patients with concentrations greater than 1200 U/mL indicated a 40 percent reduction in the selenium treated patients compared to a 10 percent increase in the placebo group.

"Selenium substitution with 200 mcg of sodium selenite may improve the inflammatory activity in patients with autoimmune thyroiditis," the researchers noted, but "whether this effect is specific for autoimmune thyroiditis or may also be effective in other organ-specific autoimmune diseases has to be investigated."

"With selenium supplementation, we may be increasing peroxidase activity, thereby lowering free radicals, which contribute to inflammation," Dr. Gasnier explained.

"Selenium supplementation may be necessary only in certain countries where selenium levels in the soil are low," Dr. Gasnier told *Doctor's Guide*. "In Europe, China and Central Africa, there is a lack of selenium

in the soil, so supplementation may be more important in these areas compared to others," she said.

Selenium & weight gain - EFR 6-4

William Evers (EVERSB@cfs.purdue.edu)
Mon, 22 Jan 1996 11:48:44 EST

Electronic Food Rap
Vol. 6 No. 4

Bill Evers, PhD, RD and April Mason, PhD
Extension Foods and Nutrition Specialists

Selenium is a mineral that is known for its antioxidant properties, but a recent preliminary study has found another benefit for the mineral. The following article discusses some of this benefit.

(Submitted by Judy Lagge, Extension graduate assistant)

From Agricultural Research, October 1995, p. 18, published by the Agricultural Research Service. By Marcia Wood, ARS

High Selenium Leads To Weight Gain

Meals rich in selenium may slow the rate at which your body burns calories, ARS researchers report.

This preliminary result is based on a 4-month study of 11 healthy men. It suggests a possible benefit to patients with wasting syndromes such as those sometimes associated with AIDS and cancer. Experimental high-selenium therapies already proposed for these patients might additionally help them stop losing weight-and perhaps even gain.

Chemists Wayne Chris Hawkes and Nancy L. Keim did their selenium study at the ARS Western Human Research Center in San Francisco. Their volunteers were age 20 to 45.

The five volunteers who ate foods high in selenium received about five times the Recommended Dietary Allowance, or RDA, of this mineral. These men gained about a pound and a half, despite the researchers' efforts to keep everyone's weight stable.

The scientists attribute the weight gain to lowered levels of one of the body's thyroid hormones, known as T3, or triiodothyronine. Levels of another thyroid hormone, T4, didn't change. The thyroid, through hormones, handles a wide array of tasks. Among them: regulating your calorie burning rate.

The six volunteers who ate foods that provided only one-fifth of the selenium RDA increased their levels of T3-the hormone that is more active than T4-and boosted their fat-burning rates. They lost about 1 pound. That amount "isn't significant for dieters," Hawkes says, "but signals the body's response to a low-selenium regimen."

The change in the T3 hormone, revealed in blood tests, was unexpected, says Hawkes, because it contradicts results from animal studies done elsewhere. Mice and rats fed low doses of selenium had less T3 and more T4. Animals and humans use selenium to convert T4 into T3.

Instead of an unappetizing liquid formula spiked with selenium, the San Francisco study offered familiar foods. Volunteers ate rice from China that was harvested from regions where the soil is either rich or poor in selenium. Beef from selenium-rich South Dakota went into the high-selenium menus; low-selenium beef from selenium-deficient New Zealand was served to volunteers on the opposite stint.

Menus included hot rice sweetened with maple syrup or marmalade for breakfast; spaghetti with meat sauce, or beef with curried rice, tomatoes, green peppers, and onions for lunch; and beef and noodle casserole or beef and rice with teriyaki sauce at dinner.

Besides meats and grains from regions where soils contain ample selenium, seafoods are also a good source of the mineral. And dairy products and vegetables provide some of this essential nutrient, too.

In addition to its interaction with thyroid hormones, selenium is a powerful antioxidant that protects cells from peroxides, an oxidation byproduct.

Selenium deficiency is rare in the United States, except for patients who are fed intravenously for a long time. Selenium toxicity, too, is uncommon. "However," cautions Hawkes, "selenium can be poisonous at only 10 times the RDA, so people shouldn't gobble selenium supplements."

Hawkes plans to conduct a lengthier study to see if the same selenium-induced changes to thyroid hormones occur-and, if they do, how long they persist.

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SILVER

Rough file:

JJ: The following study indicates that silver might be a key supplement that could suppress TED. TED (thyroid eye disease) is characterized by excessive growth of the fibroblasts at the back of the eye. This study shows that "silver ions greatly inhibited fibroblast proliferation."

Silver fits in with the cadmium hypothesis. Silver is just to the left of cadmium in the Periodic Table and excessive amounts of cadmium might suppress silver, just as excessive amounts of zinc (just above cadmium) suppress copper (just above silver). Since we've seen that copper is a suppressive mineral in the functions of the thyroid and the immune system, it is not unreasonable to suspect that silver is also involved in suppressive functions such as suppressing fibroblast growth. This is an extremely good reason for those suffering from TED to take a colloidal silver supplement (follow directions on the bottle).

Certain concentrations of the antiseptic AgNO₃, a potent broad-spectrum antimicrobial agent, exert cytotoxic effects on fibroblasts and endothelial cells which are directly related to the wound-healing process. In vitro assessment of human fibroblast cytotoxicity has proved to be a useful method for characterizing cell toxicity mechanisms of topically-applied antiseptics. In the present study human dermal fibroblasts were exposed to AgNO₃ at concentrations of 4.12-82.4 microM for 8 and 24 h. **Silver** ions greatly inhibited fibroblast proliferation and prolonged AgNO₃ exposure produced Ag-dependent cell loss. In the sequence of events occurring during our in vitro experimental model, the inhibitory action on DNA synthesis was the primary event in AgNO₃ cytotoxicity, associated with significant loss of cell protein. [silver nitrate cytotoxicity in human dermal fibroblasts.doc](#)

Female SJL (H-2s) mice developed serum IgG anti-nucleolar antibodies (ANoA) after 5 weeks treatment with 0.05% or 0.01% silver nitrate (AgNO₃) in drinking water. Five more weeks of treatment increased the ANoA titre to 3410 +/- 853 and 640 +/- 175 (reciprocal mean +/- s.e.m.), respectively. Controls receiving ordinary tap water and mice given 0.002% AgNO₃ showed no antinucleolar antibodies. The high-titre ANoA targeted a 34-kD nucleolar protein identified as fibrillarin, the major autoantigen in murine mercury-induced autoimmunity and in a fraction of patients with systemic scleroderma. Serum autoantibodies to chromatin or histones, kidney, spleen, stomach, thyroid, or skin antigens (except the nucleolus) were not found in any of the mice. There was no consistent significant increase of serum IgG1, IgG2a, IgG2b, or IgG3 concentrations after AgNO₃ treatment compared with controls. Mice treated with 0.05% AgNO₃ for 10 weeks showed a slight decrease in serum IgG1, IgG2b and IgG3 concentrations. These mice also showed a small but statistically significant increase in renal, mesangial IgM deposits, which was not accompanied by any increase in C3c deposits, whereas mice given lower doses of silver nitrate showed no significant increase in mesangial immunoglobulin immune deposits. Systemic vessel wall immune deposits were not found in any of the mice. In mice given 0.05% silver nitrate, the kidney showed the highest concentration of silver (12.2 +/- 0.09 micrograms Ag/g wet weight; mean +/- s.e.m.), followed by the spleen (8.7 +/- 1.3), and the liver (3.9 +/- 0.4). Treatment with 0.01% silver nitrate caused a different distribution of silver, with the highest concentration in the spleen (2.1 +/- 0.16 micrograms Ag/g), followed by the kidney (0.63 +/- 0.037), and the liver (< 0.29 micrograms Ag/g; mean). Silver seems to be a more specific inducer of antinucleolar/anti-fibrillarin autoantibodies than mercury and gold, lacks the general immune stimulating potential of mercury, and has only a weak tendency to induce renal immune deposits. These observations suggest that the autoimmune sequelae induced in mice by metals is dependent, not only upon the genetic haplotype of the murine strain, but also on the metal under investigation. [silver induces anti-fibrillarin autoantibodies.doc](#)

Menkes disease is a genetic disorder of copper metabolism. Copper uptake and retention assays on fibroblast or amniotic fluid cell cultures have been used for pre- and postnatal diagnosis. These copper loading tests are complicated by the use of ⁶⁴Cu, which is not commonly available and has a very short (12.8 hours) physical half life. Besides copper, **silver** is also a substrate for the bacterial homologue of the Menkes transport protein. We report here that loading tests using radioactive **silver** (^{110m}Ag), instead of copper, can be used for the diagnosis of Menkes disease. ^{110m}Ag is commercially available and has a convenient physical half life of 250 days, which makes it suitable for use in diagnostic laboratories. Our studies support the hypothesis that reduction of divalent to monovalent copper is an essential step preceding transport. [silver loading of fibroblasts in Menkes disease.doc](#)

The following study indicates abnormalities of vitamin B12, folic acid, and thyroidal function were found in workers at a silver-reclaiming factory. While the study looks at cyanide intoxication, there is the possibility that excess silver interferes with these functions.

JAMA 1985 Jan 18;253(3):367-71

Cyanide intoxication among silver-reclaiming workers.

Blanc P, Hogan M, Mallin K, Hryhorczuk D, Hessel S, Bernard B

Thirty-six former workers in a silver-reclaiming facility who had been exposed over a long-term to excessive levels of cyanide were studied to determine acute and residual toxic reactions. The study involved physical examinations, laboratory studies, and a questionnaire to determine levels of exposure, symptoms during employment, and current symptoms. Questionnaire data showed that during the time of active employment there was a high prevalence of symptoms that are consistent with acute cyanide toxic reactions. A significant positive trend for prevalence of cyanide-related symptoms measured against levels of exposure was demonstrated, supporting a dose-response effect. Some symptoms occurring seven or more months after exposure had ceased also exhibited a dose-response trend. Mild abnormalities of vitamin B12, folate, and thyroid function were detected and suggest long-term cyanide effects.

Letter from group member:

John and others:

i have had positive results from colloidal silver for other ailments. i have come to believe that it is very good stuff! originally i had read that

something like 1/3 of all adults have parasites and don't know it. the germophobe that i am i was immediately convinced that i had parasites and looked up how to naturally get rid of them. colloidal silver and garlic. i have also used colloidal silver when i am coming down with the flu and feel like i am going to throw up. boom, no more flu. also, my boyfriend gets psoriasis sp? really bad (rough, flaky skin patches) and topically applied colloidal silver and all but got rid of his patches (and hardly anything else has worked in the past). i am not trying to sell the stuff, i just wanted to point out that colloidal silver has many benefits... probably way more that we know. plus, not that this is proof and may not even be connected, but i have taken this stuff on and off and have not shown signs of TED, while my sister, years ago, got TED. maybe the silver helped me, and i even smoked. (not anymore though :)) !!!!
Mary Margaret

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Do you think you might have thyroid disease but aren't sure? Here is a description of the symptoms of hypothyroidism (Hashimoto's Thyroiditis), hyperthyroidism (Graves' Disease), and Ophthalmopathy or Thyroid Eye Disease (TED). If you're still not sure, get to a doctor and have a thyroid panel done. If the thyroid panel doesn't show elevated or depressed hormone levels, consider other options such as hypertension or Pheochromocytoma.

GRAVES' DISEASE/HYPERTHYROIDISM SYMPTOMS

1. **Rapid Heart Rate, often first noticeable about 4-6 am.**
2. **Sweating, trembling, and feeling hot.**
3. **High libido.**
4. **Rapid loss of weight and muscle strength.**
5. **Inability to exercise because of rapid heart rate.**
6. **Significant increase in heart rate when frightened which doesn't decrease as normal.**
7. **Itching or protruding eyes (beginning of TED, thyroid eye disease.**
8. **Inability to think clearly, or brain fog.**
9. **Psychiatric problems associated with the above symptoms.**
10. **Thyroid storms which are periods of severe rapid heart beat which makes you wonder if you're going to live or die.**

Hyperthyroidism is a very serious situation and life threatening. People die every day of it. If you are having thyroid storms, you need to get to a doctor as soon as possible. You are in real trouble and could die of a heart attack. If it is an emergency and you cannot get to a doctor or secure proper medication, take calcium and magnesium in a 1:1 ratio (take extra magnesium if necessary), or take only magnesium if no calcium is available. You may need to take 6-12 capsules to control a thyroid storm. Also read the foods not to take as these can precipitate a thyroid storm.

The antithyroid medications are not dangerous for most people. They carry some risk for long-term use, but many people have been taking them for over 20 years. Once on the antithyroid drugs (ATDs) you can begin a supplement program. I believe that by supplementing with copper and the other nutrients in the Supplement List that you should gradually recover and be 80-95% recovered in three months. If you have had hyperthyroidism for a long time, recovery will probably take longer.

HASHIMOTO'S THYROIDITIS/HYPOTHYROIDISM

1. **Low energy.**
2. **Depression.**
3. **Low libido.**
4. **Feeling cold and having a subnormal body temperature.**
5. **Gaining weight.**
6. **Getting a round face.**
7. **Developing a yellow tint to the skin, from being unable to convert beta carotene into vitamin A.**
8. **Low pulse rate.**
9. **Inability to think clearly, or brain fog.**
10. **Irritability.**

If you have any of the above symptoms, you should get to a doctor and get a blood sample taken to determine thyroid hormone levels. Many people, especially women, are misdiagnosed and told that they are depressed, or that "it's all in your head." Demand a thyroid test so that you will know.

(This area under construction. Please come back soon.)

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THYROID EYE DISEASE (TED)

Thyroid eye disease (TED) is one of the stranger aspects of thyroid disease and particularly interesting from three reasons: first, it is such a bizarre phenomenon making the investigation very interesting; two, it provides some very interesting clues about what causes it and what causes Graves' disease; and third, it can be extremely uncomfortable for the person suffering from it and this makes finding a cure very motivating.

TED is also known as ophthalmopathy, orbitopathy, or exophthalmia. The eyes bulge out and if this becomes severe enough the eyelids no longer close, causing the eye to dry out. Sufferers may have to tape their eyes shut at night to keep their eyes from becoming dry and damaged.

The cause of this bulging of the eye is the growth of fibroblasts at the back of the eye. This tissue grows so much that the eye is pushed outward. Even more interesting is that there is often another growth in the same person--the tissue at the front of the shin, which is also full of fibroblasts, grows and this thickened skin is called pretibial myxedema. This myxedema is sometimes found on the corresponding underside of the lower arm and at other places in the body.

Interestingly, Graves' patients are not the only ones which get TED and pretibial myxedema. People with Hashimoto's thyroiditis also get it and even some people who don't have obvious thyroid dysfunction may get it.

Scientists don't know for sure what causes this fibroblast growth, but studies show that the immune system seems to be involved. Immune system agents called immunoglobins seem to stimulate the growth of the fibroblasts. The same antibodies that seem to cause Graves' and Hashimoto's seem to be the ones involved.

One of the fascinating clues about the cause of Graves', TED, and possibly Hashimoto's is that smokers are more likely than nonsmokers to get all of these conditions. There seems to be something ingested in the tobacco smoke that causes these conditions to develop and worsen.

While there are many substances in tobacco smoke which affect the thyroid, most of these seem to have short-lived effects. I believe that the agent in tobacco which causes thyroid disease must stay in the body a long time.

My theory is that the agent in tobacco smoke which stimulates the onset of Graves' and TED is cadmium. Cadmium is a very toxic heavy metal which is found in the Periodic Table of Elements right below zinc, which in turn is just to the right of copper.

Cadmium is a metal found naturally in soil which is taken up by green leafy plants such as tobacco. Other green leafy plants like lettuce, spinach, beet greens, and Swiss chard also are high in cadmium. Some root vegetables like carrots seem to accumulate cadmium. The fact that cadmium is taken up by these plants and humans and other animals eat and enjoy these plants suggests that cadmium might be an essential nutrient.

There is a protein in the body called metallothionein, which is formed from the amino acid cysteine, that transports cadmium, zinc, copper and possibly other metals in the body. It's possible that excessive cadmium competes for transport sites with copper and zinc and may even be preferentially transported by metallothionein and this is the reason why cadmium in excessive amounts is so toxic to the body.

Cadmium is a very useful metal because it provides corrosion resistance and has electrical properties. It is used extensively in industry and cadmium waste goes into the sewage system. Sewage sludge is an inexpensive fertilizers used in agriculture. Because of growing awareness of the high cadmium content and the dangers of cadmium are becoming more well known, most progressive and organic farmers do not use sewage sludge. However sewage sludge is still used in some agriculture. Tobacco is one of the crops which are fertilized extensively with sewage sludge, and this is one reason why tobacco is so high in cadmium. However, even tobacco not fertilized this way has high cadmium because the plant naturally accumulates cadmium from the soil. When tobacco is smoked, relatively large amounts of cadmium are ingested into the body.

Batteries are another source of cadmium. Ni-Cad or nickel-cadmium batteries are used extensively and we all handle these. It is highly likely that cadmium particles cling to the outside of these batteries and we may ingest this cadmium if we don't thoroughly wash our hands after handling these batteries.

There are some very big problems with cadmium entering the body. First of all, cadmium is known to be toxic to the thyroid gland cells. Thyroid cells can be taken from an animal and put into a dish and kept alive. Then various substances including heavy metals can be added to the cells to study the effects. From these studies cadmium has been determined to be a metal which is particularly damaging to thyroid cells. It's not surprising that smoking might cause thyroid malfunction.

Another interesting thing about cadmium is that female animals tend to accumulate cadmium while male animals tend to not accumulate it as much. This is an extremely strange phenomenon but it lends support to the theory that cadmium is a culprit in autoimmune thyroid disease and TED.

Consider these experiments: Scientists took male and female rats and castrated them, thereby eliminating the bulk of their naturally produced sex hormones, testosterone and estrogen. Then they gave half the animals (both male and female) cadmium. The groups were further divided so that half of each group was injected with testosterone and half with estradiol (the most potent of the estrogens). The animals that were given estradiol, whether male or female, were found to accumulate cadmium, and the animals given testosterone were found to excrete the cadmium. By this experiment it was shown that estrogen (estradiol) causes the accumulation of cadmium, while testosterone causes the excretion of cadmium.

What does this mean? It means that women are much more likely to accumulate cadmium and to suffer from the toxic effects of cadmium. (I will discuss this situation in more detail in the cadmium story.) Since women make up close to 90% of thyroid disease cases, this offers very suggestive evidence that cadmium might be an important factor. Women's bodies are not well suited for being exposed to toxic metals.

Another interesting aspect of TED is that studies show that TED increases following radioiodine therapy (RAI). When you think about it, this is a very strange, but intriguing phenomenon also.

My feeling is that this might also be connected to cadmium. When radioactive iodine is administered in RAI, we know that this radioiodine must break down into alpha particles and other elements. Iodine is element number 53, so when it breaks down it presumably breaks down into elements with smaller atomic numbers.

Cadmium is element number 48, only five elements below iodine. It's possible that as radioiodine breaks down into cadmium which is the stable breakdown product. I hope to find out if this is possible, but this would fit in with the observations and theory that cadmium toxicity is a prime cause of TED and Graves'.

If the theory that cadmium toxicity is a major causative factor in TED and Graves', then there is another bizarre conclusion: that consumption green leafy vegetables might be very damaging to sufferers of Graves' and TED. I have to laugh every time I think about this because it is a very strange conclusion. It's extremely difficult for me or most people to think of salads filled with green leafy vegetables as possibly being culprits in Graves'.

Remember that this is just a theory, but interestingly this agrees with my experience when I had hyperthyroidism. It seemed that whenever I ate a green salad my hyper symptoms would increase and that night would be a more difficult night than usual.

Also, recently I met a woman who was the first person I've known with TED. I was amazed at how her eyes protruded and she told me that she had just concluded a series of ten radiation sessions in which the radiation was directed to the fibroblasts at the back of the eyes. I felt very sorry for her—it's not a pretty sight.

I explained many of my theories to her including the one about how eating green leafy vegetables might be very damaging because of the cadmium content. I was very amazed when she told me that she practically lived on salads loaded with green leafy vegetables. This is just observation, but it didn't contradict the theory. Pretty strange theory, if true.

March 5, 2002

Some group members have said that flax seed oil or eggs from chickens fed flax seed oil have benefited their thyroid eye disease. It's definitely worth a try.

STUDIES

The following study may be extremely significant for the understanding of Graves' disease and Graves' ophthalmopathy (TED). While I hesitate to jump to conclusions, this study seems to indicate that manganese superoxide (MnSOD), which is an antioxidant, may stimulate retroocular fibroblast growth which is the root of TED. The retroocular fibroblasts seem to grow in response to stimulation by the TSH receptor antisera (anti-p1). MnSOD has a similar structure to the TSH receptor peptide and apparently in Graves' there is an autoimmune response to MnSOD. Therefore it is possible that an excess amount of manganese in the diet causes excessive production of MnSOD which in turn causes an autoimmune response to MnSOD and this stimulates the retroocular fibroblasts. While this would be very interesting, I don't know if my interpretation of this is correct. However, this does fit in with the fact that manganese is a copper antagonist and high levels of manganese would suppress copper levels. Copper supplementation could, in turn, help reduce manganese levels and help suppress this autoimmune response.

Immunodetection of manganese superoxide dismutase in cultured human retroocular fibroblasts using sera directed against the thyrotropin receptor.

Burch HB, Barnes S, Nagy EV, Sellitti D, Burman KD, Bahn RS, Lahiri S

Endocrine-Metabolic Service, Kyle Metabolic Unit, Walter Reed Army Medical Center, Washington, DC 20307-5001, USA.

The identification of antigenic targets in the retroocular autoimmune response of Graves' ophthalmopathy is likely to increase our understanding of mechanisms underlying this disorder. While a number of putative autoantigens have been identified on the basis of molecular weight or cell of origin, a determination of the significance of these antigens is contingent upon an identification of the amino acid sequence. Our group has previously identified **immunoreactive retroocular fibroblast (ROF) proteins recognized by thyrotropin receptor (hTSH-R) antisera (anti-p1)**, at molecular weights of 95, 71, 41, and 14-25 kDa. In the present study, proteins detected by anti-p1 and visualized by Ponceau staining were isolated and processed for microsequencing. Ponceau staining revealed dense bands at molecular weights of 14 and 23

kDa, and a weak band at 41 kDa. N-terminal sequencing was performed on the prominent band at approximately 23 kDa, showing it to be manganese superoxide dismutase (MnSOD), a mitochondrial enzyme responsible for protection against oxygen free radical-associated cellular damage. **Sequence comparison of MnSOD to the hTSH-R peptide, p1, revealed a linear segment of amino acid homology.** Preincubation of anti-p1 with p1 blocked immunodetection of the 23 kDa band corresponding to MnSOD, and immunoprecipitation of ROF protein using anti-p1 yielded protein recognized by anti-MnSOD. **Autoimmunity against human recombinant MnSOD was further assessed by ELISA. Patients with Graves' disease (n = 53) had significantly higher ELISA indices than normal control subjects (n = 29), while patients with Hashimoto's thyroiditis had intermediate values.** These results document MnSOD autoantibodies in patients with Graves' disease and suggest that this may result from an immune cross-reactivity between MnSOD and the TSH-receptor.

The following study suggests that selenium deficiency is involved in fibrosis. This proliferation of fibroblasts is also seen in Thyroid Eye Disease, therefore this condition may be a result of selenium deficiency.

Title

***Selenium* deficiency and thyroid fibrosis. A key role for macrophages and transforming growth factor beta (TGF-beta).**

Author

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Source

Mol Cell Endocrinol, 124(1-2):7-15 1996 Nov 29

Abstract

Free radical damage and fibrosis caused by *selenium* deficiency are thought to be involved in the pathogenesis of myxoedematous cretinism. So far, no pathway explains the link between *selenium* deficiency and tissue fibrosis. Pharmacological doses of iodine induce necrosis in iodine-deficient thyroids. Necrosis is much increased if the glands are also *selenium*-deficient, which then evolve to fibrosis. This rat model was reproduced to explore the role of *selenium* deficiency in defective tissue repair. At first, proliferation indexes of epithelial cells and fibroblasts were comparable between *selenium*-deficient and control groups. Then, in *selenium*-deficient thyroids the inflammatory reaction was more marked being mainly composed of macrophages. The proliferation index of the epithelial cells decreased, while that of the fibroblasts increased. These thyroids evolved to fibrosis. TGF-beta immunostaining was prominent in the macrophages of *selenium*-deficient rats. Anti TGF-beta antibodies restored the proliferation indexes, and blocked the evolution to fibrosis. In *selenium* deficiency, an active fibrotic process occurs in the thyroid, in which the inflammatory reaction and an excess of TGF-beta play a key role.

The following is a study which suggests that a bone marrow transplantation cured Graves', TED, and anemia. This could also be interpreted that the Graves' and TED were caused by the anemia and correction of the anemia by the bone marrow transplantation corrected these conditions. The bone marrow is where the red blood cells are manufactured. Be aware that this is just one case and not scientific evidence.

Clin Endocrinol (Oxf) 1999 Feb;50(2):267-70

Apparent cure of Graves-Basedow disease after sibling allogeneic bone marrow transplantation.

Diez S, Baniias H, Diez-Martin JL, Briz M, Estrado J, Barcelo B

Department of Endocrinology, Universidad Autonoma, Madrid, Spain.

Evidence that allogeneic bone marrow transplantation (BMT) can cure or alter the course of intractable autoimmune diseases comes from both extensive experimental work in animal models and anecdotal case reports in humans. We describe a female patient diagnosed as having severe aplastic anaemia (SAA), hyperthyroidism and ophthalmopathy of Graves-Basedow disease who received a BMT from her histocompatible sister. Fifty-three months after BMT, complete remission of hyperthyroidism and ocular signs persists. The SAA is cured and she is free of any chronic graft-versus-host disease (GVHD). In the early post-BMT period, PCR analysis of bone marrow and peripheral blood cells confirmed a complete chimerism of donor origin. Thus, it is plausible to attribute the resolution of the patient's thyroid hyperfunction and ophthalmopathy to the replacement of the host immune system.

PMID: 10396372, UI: 99324694

The following study shows that radiation therapy for ophthalmopathy (TED) does not produce any beneficial effects that can be measured (by the methods used in this test). There does not seem to be any benefit from radiotherapy, leaving only the negative effects of radiation. I see absolutely no reason to undergo radiation therapy for TED.

A PROSPECTIVE, RANDOMIZED, DOUBLE-BLIND CONTROLLED STUDY OF ORBITAL RADIOTHERAPY FOR GRAVES' OPHTHALMOPATHY.

C. Gorman, J. Garrity, V. Fatourech, R.S. Bahn, I. Petersen, S. Stafford, J. Earle, G. Forbes, R. Kline, E. Bergstralh, K. Offord, D. Rademacher, N. Stanley and G. Bartley Division of Endocrinology and Departments of Ophthalmology, Radiation Oncology, Diagnostic Radiology and the Section of Biostatistics, Mayo Clinic, Rochester, Minnesota USA and University of California Davis at Sacramento, Division of Radiation Oncology, Sacramento, California USA

Background: Although widely used for treatment of Graves' ophthalmopathy (GO), the efficacy of orbital radiotherapy (OT) has not been established in a prospective randomized double-blind controlled trial.

Specific aims: To determine: 1) If 20 Gy of external beam OT directed to one orbit of patients with GO resulted in improvement in comparison with the untreated orbit when evaluated three and six months after therapy; 2) If 20 Gy of OT to the second orbit six months later produced effects similar to those observed when the first orbit was treated; 3) To relate the magnitude of the treatment effect to the time since onset of eye symptoms.

Patients and Methods: Forty-two euthyroid patients with mild to moderate GO and elevated TSI levels received 20 Gy of megavoltage radiation to a randomly selected orbit. Six months later the second orbit was treated. Every three months, measurements were made of thyroid function and antibody status, proptosis, volume of extraocular muscle (EOM) and fat, range of EOM motion, eyelid fissures and extent of diplopia. The study had 80% power to detect 0.5 mm change in proptosis and 0.75 mL in volume measures.

Results: Six month - baseline measurements were recorded for the untreated (UT) and the treated (T) orbit. They revealed (mean±SD): Fat volume(cc) UT -0.3(1.3), T 0.3(1.3), P 0.87. Muscle volume(cc) UT -0.4(1.3), T -0.6(1.4), P 0.14. Proptosis(mm) UT 0.0(1.0), T -0.1(1.3), P 0.46. Range of motion area (cm²) UT 8.7 (33), T 8.8(35), P 0.98. Lid fissures(mm) UT 0.0(2.0), T -0.1(1.7), P 0.42.

Results at three months were similar to those at six months. Diplopia field area at baseline, six and 12 months was 42, 41, and 39 cm². P=0.09 for six months - baseline and 0.02 for 12 months - baseline. Subset analyses of early vs. late treated orbits, or smokers vs. non-smokers, and of patients treated <1.3 vs. >1.3 years since onset disclosed no significant differences for any group.

With one exception, patients were euthyroid on commencing and throughout the study.

Conclusion: If radiotherapy is beneficial for Graves' ophthalmopathy, its ameliorative effects did not reach the detection level of the techniques used in this study. No clinically significant benefit was observed.

From Mercola.com:

Radiotherapy Does Not Help Graves' Disease Eye Problems

For years, radiation therapy to the eye has been used to treat eye problems associated with the thyroid condition Graves' disease. Now a new study questions **whether this treatment is actually useful**.

Graves' disease triggers an overproduction of hormones from the body's thyroid gland, a key regulator of metabolism and other vital functions. A small percentage of people with the disorder have a complication called Graves' ophthalmopathy, which is characterized by bulging eyes, double vision and other eye problems.

To investigate the effectiveness of radiotherapy for these eye complications, investigators studied 42 patients with Graves' ophthalmopathy. The patients exhibited a variety of symptoms including higher-than-normal volumes of eye muscle and fat, bulging of the eyes, less eye range of motion and double vision.

The patients received radiotherapy in one eye and a "sham" treatment in the other eye.

At follow-up, 3 and 6 months after treatment, **no significant differences were observed between the treated and untreated eyes**.

And this was true regardless of whether a patient was a smoker. **Smokers**, the researchers note, have been found to be **more vulnerable** to Graves' ophthalmopathy, and this could theoretically affect their response to treatment.

Graves' disease is a naturally remitting condition, and over a period of time many of the symptoms, including [those related to] the eyes, may improve. This tendency to natural remission, together with the imprecision of measurements used in most previous studies, has allowed the perception to persist that the treatment is effective.

Overall, in 44% of the patients, the eye treated with radiotherapy did not appear any different from the non-treated eye. In about **27% of patients the treated eye appeared better** than the untreated eye, but in **30% it appeared worse**.

Ophthalmology September 2001;108:1523-

If you look at the following study you'll see that a significant improvement was obtained in TED (Graves' ophthalmopathy) with vitamin B3 (nicotinamide--a form of niacin). 300 mgs of nicotinamide a day was used. Allopurinol is an inhibitor of xanthine oxidase. Xanthine oxidase is a molybdenum-based enzyme. Since molybdenum and copper are antagonists, a copper deficiency could allow excess xanthine oxidase to proliferate. If xanthine oxidase is involved in the genesis of TED, then this is a possible explanation of why copper might help reduce TED.

The significance of this study is that it really offers evidence that TED is a nutritional deficiency disease.

A note on molybdenum: it's possible that excess molybdenum is involved in TED. If you have TED and are trying molybdenum, be especially aware to see if molybdenum might increase the symptoms of the TED.

<<<http://forums.about.com/n/main.asp?webtag=ab-thyroid&msg=11222.1&Find=Find>

Am J Ophthalmol 2000 May;129(5):618-22 Related Articles, Books, LinkOut

Antioxidant agents in the treatment of Graves' ophthalmopathy.

Bouzas EA, Karadimas P, Mastorakos G, Koutras DA Department of Ophthalmology, Red Cross Hospital, Athens, Greece.
mastorak@matrix.kapitel.gr

PURPOSE: To report the effect of antioxidant agents in the treatment of mild and moderately severe Graves' ophthalmopathy. **METHODS:** Prospective, nonrandomized, comparative study performed at a referral center. A series of 11 patients with mild or moderately severe, active, newly diagnosed Graves' ophthalmopathy were included in the study. Allopurinol (300 mg daily) orally and nicotinamide (300 mg daily) orally were used for 3 months. A complete ophthalmologic examination was performed before and 1 and 3 months after initiation of treatment. The response to treatment was estimated separately for each component of the disease and overall by its effect on a total eye score. Eleven patients with mild or moderately severe, active, newly diagnosed Graves' ophthalmopathy who received placebo were also examined at the same time points. Patients in each group were recruited consecutively. Although nonsmoking was not an exclusion criterion, all patients were cigarette smokers. **RESULTS:** Nine (82%) of 11 patients treated with oral antioxidants showed improvement of mild to moderately severe Graves' ophthalmopathy versus three (27%) of 11 patients in the control group ($P < .05$). Soft tissue inflammation was the component of the disease that responded more to treatment. No side effects of antioxidant treatment were recorded. Patients' satisfaction was high. **CONCLUSIONS:** This pilot study presents encouraging results in the treatment of mild and moderately severe Graves' ophthalmopathy with antioxidant agents. To evaluate these preliminary results, randomized prospective studies are needed.

Mary Shomon told me about a website called www.TEDCURE.com.

When potassium is deficient the cell membrane allows more water to enter the cell than escape so cells swell up with water. This is manifested in people as edema and many hypothyroids report gaining weight on very little calorie intake and generally having edema. Myxedema which is another form of edema and which is seen in Graves' as pretibial myxedema or orbital fibroblast proliferation may have the same origin: from potassium deficiency. I consider it quite likely that potassium deficiency is a major contributing cause to TED and worthy of further investigation. However, I doubt if potassium deficiency is the only cause. Most likely it is one of several deficiencies whose combination leads to the condition.

Following is a list of potassium deficiency symptoms from Dr. Gupta's website:

HEAD	: heavy; lethargy, drowsy, yawning, mild headache; dull thinking & concentration, emotional, Hairs slowly turning grey with weak roots.
EYES	: heavy; tired, photophobia.
EARS	: buzzing.
NOSE	: irritation & repeated sneezing.
FACE	: abnormal feel of superficial skin.
MOUTH	: dry; gum bleeding, recurrent cuts inside the mouth while eating; side of tongue having abnormal feel, hiccups & reflux oesophagitis; hoarse voice.
NECK	: muscles tired as while driving; jerky movements at neck.
UPPER LIMBS	: cold hands; arms tired while working; numbness & tingling of hands; corns on fingers; arms & hands as if falling down when outstretched; grip not strong & handwriting not clear with less pressure while writing; bilateral tender points near elbows; visible pulsating vessels.
BACK	: itchy; often lumbar sprains.
HEART	: pulsation & palpitations; high recordable B.P.
CHEST	: rapid breathing; suffocation while lying down.
ABDOMEN	: constipation; excessive gas formation & urination.

LOWER LIMBS : painful buttocks while prolonged sitting on hips; pain in thigh muscles while going upstairs & pain in lower leg muscles while sitting on foot; bilateral tender points on lower legs near ankles; stamping gait multiple corns; cold & numb feet.

JOINTS : pain on pressing joint crease.

WHOLE BODY : as if squeezed out, with the desire to lie down; dull & apprehensive;
And History of falling down on ground.

This problem of K-loss results in early maturity, early decay and early death.

The following study shows that smoking and RAI greatly increase the risk for developing Thyroid Eye Disease. Also note

Risk factors for thyroid optic neuropathy include smoking, radioactive iodine treatment

Patients should be followed closely. Visual-field and color-vision testing help in early detection.

by Bob Kronemyer

May 15, 1999

photograph

---**Disk edema in a** patient with thyroid optic neuropathy and field defect.

WAIKOLOA, Hawaii — Smoking and radioactive iodine treatment alone are two risk factors for developing thyroid optic neuropathy among patients with Graves' hyperthyroidism.

"We now know that smoking is a significant risk factor," said Robert L. Lesser, MD, a neuro-ophthalmologist in private group practice in Waterbury, Conn. "This is another reason to warn these patients that

they should not be smoking. In fact, patients who have thyroid disease in general are seven times more likely to develop a more severe form of ophthalmopathy if they smoke."

Combined treatment may be better

photograph

---**Clinical photograph of** a patient with marked limitation of gaze with thyroid optic neuropathy and minimal proptosis.

Radioactive iodine treatment alone also increases the risk of contracting or worsening ophthalmopathy. One study published last year showed that 15% of patients who were treated only with radioiodine developed or had worsening ophthalmopathy. In contrast,

none of the patients who were treated with both radioiodine and prednisone had progression, and two-thirds showed improvement. Further, only 3% of those treated with methimazole had any worsening of eye disease.

"Presumably what happens with thyroid ophthalmopathy is that the lymphocytes that are targeting against the thyroid also react to the eye muscles. You end up with lymphocytic infiltration and mucin deposition," said Dr. Lesser, who spoke here at Hawaii '99, sponsored by *Ocular Surgery News* and the New England Eye Center.

The inferior rectus, medial rectus and superior rectus are the most commonly involved muscles, "so it is really an eyeball diagnosis," said Dr. Lesser, who recommends "a computerized tomography [CT] scan or magnetic resonance imaging [MRI] of the orbit with fat suppression to document enlargement of the muscles."

Dr. Lesser cited a female patient with white eyes. "That doesn't necessarily make a difference, though. Sometimes the eyes are congested and sometimes they are not," he said. However, the patient also had minimal proptosis. "That is one of the tip-offs that there is a greater risk for thyroid optic neuropathy, be cause of the simple mechanical crowding phenomenon."

Although the risk of developing the disease is relatively low (1% to 5%), vision loss is possible; therefore, these patients should be tested and followed closely. Moreover, the absence of disk edema does not exclude the diagnosis.

Test useful for early detection

Visual-field and color-vision testing help in early detection. "Patients need to be alerted about the

possibility of a change in vision and need to arrange to see you if this happens,” Dr. Lesser said. Low-dose radiation may be appropriate for even some of the congestive findings.

Once the diagnosis is made, Dr. Lesser starts patients on short-term steroids. “I do not favor using steroids on a long-term basis because I think the treatment becomes worse than the disease,” he said. He also mentioned that high-dose steroids may be appropriate in certain situations. “We are now becoming comfortable with 1 g of methylprednisolone intravenous for 3 to 5 days and seeing if that rapidly decompresses the muscle.”

Dr. Lesser’s patients are maintained on steroids throughout radiation treatment. “It is at that point that I taper the steroids and then measure the effect,” he said. “Results are quite good in most cases.” Surgical decompression of the orbit is reserved for those patients with a contraindication or intolerance. “You have several choices with decompression, including lateral wall, medial wall and inferior wall,” he said.

Overall, patients are “psychologically devastated” by thyroid orbitopathy, Dr. Lesser said. “A lot of these patients need counseling and support.”

For Your Information:

- Robert L. Lesser, MD, can be reached at 1201 W. Main St., Waterbury, CT 06708; (203) 597-9100; fax: (203) 597-1696. Dr. Lesser has no direct financial interest in any of the products mentioned in this article, nor is he a paid consultant for any companies mentioned.

Reference:

- Bartalena L, Marcocci C, Bogazzi F, et al. Relation between therapy for hyperthyroidism and the course of Graves’ ophthalmopathy. *N Engl J Med*. 1998;338(2):73-78.

WAIKOLOA, Hawaii — Smoking and radioactive iodine treatment alone are two risk factors for developing thyroid optic neuropathy among patients with Graves’ hyperthyroidism.

“We now know that smoking is a significant risk factor,” said Robert L. Lesser, MD, a neuro-ophthalmologist in private group practice in Waterbury, Conn. “This is another reason to warn these patients that they should not be smoking. In fact, patients who have thyroid disease in general are seven times more likely to develop a more severe form of ophthalmopathy if they smoke.”

Blindness following orbital irradiation for Graves' ophthalmopathy.

Arch Ophthalmol. 1984 Oct;102(10):1473-6.

Radiation retinopathy after orbital irradiation for Graves' ophthalmopathy.

Kinyoun JL, Kalina RE, Brower SA, Mills RP, Johnson RH.

Recent reports indicate that orbital irradiation for Graves' ophthalmopathy is sometimes beneficial, particularly for dysthyroid optic neuropathy, and is not associated with serious complications. We are aware, however, of four patients who were found to have radiation retinopathy after orbital irradiation for Grave's ophthalmopathy. All four patients have decreased central acuity, and three of the four are legally blind in one or both eyes. Computer reconstruction of the dosimetry, based on computed tomography and beam profiles, shows that errors in dosage calculations and radiotherapy technique probably account for the radiation retinopathy in three of the four patients. Radiotherapy for Graves' ophthalmopathy should be administered only by competent radiotherapists who are experienced in the treatment of this disease. Similar errors in dosage calculations and treatment techniques may account for other reports of radiation retinopathy after reportedly safe dosages.

Publication Types:

- Case Reports

PMID: 6548374 [PubMed - indexed for MEDLINE]

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TESTS AND DRUGS

Under construction is a page describing the various drugs used for the treatment of thyroid disease (click on Drugs at left):

- **Antithyroid drugs for hypers:** PTU, Tapazole, Methimazole etc.
- **Thyroid hormone replacements:** Armour, Synthroid, and Levo-Thyroxin.

Laboratory Tests for Thyroid Function

By Elaine A. Moore

Normally, the thyroid gland pumps enough thyroid hormone into the blood to cover all of the body's needs. Thyroid hormones include T4 (tetraiodothyronine, thyroxine) and T3 (triiodothyronine). T4 and T3 circulate in the blood primarily bound or linked to protein molecules. Thyroid carrier proteins include thyroxine binding globulin (TBG), albumin, or transthyretin (TTR). Linked to these proteins, thyroid hormone isn't available to the body's cells.

Measurement of this protein bound thyroid hormone is referred to as a "total" level. Total T4 and to a lesser extent total T3 levels are affected by the concentrations of protein in the blood. Certain medications, hormones such as estrogen, other non-thyroidal illnesses and liver problems can cause alterations in protein concentration. Influenced by protein alterations, the total T4 and T3 measurements may not accurately represent thyroid function.

The free or unbound portion (free T4 or FT4 and free T3 or FT3) more accurately represents what the body's true thyroid hormone levels are. Levels of free hormone represent the active hormone available to react with cell receptors in the body.

Certain circumstances, including stress, trauma, medications, infections, and temperature fluctuations change the amount of thyroid hormone required by the body. The hypothalamus in the brain ensures that normal levels are maintained via a negative feedback mechanism. The hypothalamus releases a hormone known as thyrotropin releasing hormone (TRH) when it detects low levels of thyroid hormone in the blood. TRH, in turn, causes the pituitary to release a hormone known as thyrotropin or thyroid stimulating hormone (TSH). As its name implies, TSH stimulates the thyroid gland to produce and release more thyroid hormone into the blood circulation.

When blood levels of thyroid hormone are low (in hypothyroidism), the pituitary produces and releases excess TSH, and blood levels of TSH rise above the normal range. In hyperthyroidism, a condition of excess blood thyroid hormone, the hypothalamus orders the pituitary to stop releasing TSH, and blood TSH levels are low, often suppressed to levels < 0.01 mIU/L.

Although TSH is considered a valuable indicator of thyroid function, its results can be misleading. TSH levels as a measurement of thyroid function were originally designed to detect chronic cases of hypothyroidism or hyperthyroidism. However, it generally takes 6 weeks for TSH levels to reflect the status of thyroid hormone in the blood. This is because TSH is normally released in a pulsatile fashion, peaking during the night, and the changes in response are subtle, with TSH gradually responding to excess or diminished thyroid hormone. In patients undergoing medication changes or who are undergoing treatment for hyperthyroidism, TSH levels may take many weeks to many months to reflect thyroid hormone changes.

Thus, patients with abnormal thyroid function or abnormal thyroid hormone levels may have normal TSH levels in the early stages of thyroid dysfunction and after medication and treatment changes. For this reason, a FT4 and/or FT3 determination is also recommended.

The thyroid gland produces primarily T4 with only scant amounts of T3. The majority of T3 present in the blood is produced by conversion of T4 to T3 in peripheral (away from the thyroid) tissue, primarily the liver. Selenium deficiency, certain medical disorders, and certain medications suppress the conversion of T4 to T3, and it is important that levels of FT3 be measured in patients exhibiting symptoms of hyperthyroidism and hypothyroidism and normal T4 results.

Reference ranges for laboratory tests are established by testing a segment of the normal population, generally hospital workers, and averaging their results. For thyroid patients undergoing treatment, there are flaws in comparing patient results to this reference range.

There is a recent trend to discount TSH results and treat patients on the basis of their actual free thyroid hormone levels or their symptoms.

The following reference ranges represent commonly used thyroid function reference ranges. However, ranges and units of measurement may vary from one laboratory to another. Patient results must be compared to the reference range of the appropriate testing facility.

Adult Reference Ranges:

T4 = 5.6-13.7 ug/dl (mcg/dl)

FT4 = 0.8-1.5 ng/dl

T3= 87-180 ng/dl

FT3 = 230-420 pg/d;

TSH = 0.4-4.5 mIU/L (mU/L)

Copyright, Elaine A. Moore, July, 2000.

Medical Treatments for Graves' Disease

[Posted 4-14-00: Elaine Moore's excellent article on Current Medical Treatments for Graves'. Click here on Medical Treatments for Graves'.](#)

SHOULD WE SCRAP THE TSH TEST ENTIRELY?

Dr. David Derry thinks so. In this interview, he looks at the real history of thyroid testing, and why he believes "the TSH [test] needs to be scrapped and medical students taught again how to clinically recognize low thyroid conditions." Find out more about his provocative ideas and why he thinks it's time for a return to a more valid way of diagnosing and treating thyroid disease.
<http://thyroid.about.com/library/weekly/aa072500a.htm>

Other notes: don't get scared when the doctor says things like:

- (1) **"You have nodules and we have to check to see if they are cancerous."** Thyroid cancer is extremely rare and is probably also correctable through nutrition.
- (2) **"We need to do a RAIU (radio iodine uptake test)."** It doesn't do any good that I can see and may cause problems.
- (3) **"Your ultrasound shows definite structural abnormalities in your thyroid gland."** This is what my doctor said to me and I got a little scared, but everything corrected just fine.
- (4) **"We need to do a fine-needle aspiration (FNA) on your thyroid."** This involves sticking needles into your thyroid to get tissue samples. I'd really avoid this insult to your thyroid. Some people have really bad reactions to this procedure and it doesn't matter what they find—it doesn't help your thyroid.
- (5) **"We need to do a _____ test."** My advice is to avoid all tests and procedures. They don't help the situation. There's only one way to correct the underlying problem that creates hyperthyroidism: nutritional correction. Every other method treats symptoms and doesn't correct the causes.

FNA or Fine Needle Aspiration

Some people have reported problems following FNA, so I don't encourage anyone to have it done. However, there is always the concern that the problem with the thyroid might be cancer. Thyroid cancer is rare and usually doesn't spread to other body organs, but it is a concern.

Here is an eloquent description of what it's like to go through the procedure.

I just wanted to update you all, and especially for those that are about to undergo a FNA/FNAB. I had mine done yesterday. I was not given any freezing or anything to numb the sensation. The doctor inserted a needle in both the lower and upper nodule parts of my left side thyroid goiter. Two long jabs! It really hurt, but didn't last very long. I did feel a bit woozy afterwards, and my blood pressure dropped a bit. At least I was laying down and it was an outpatient thing. Doctor seemed in a rush, but I think he did this many times before.

The color of the sample was dark, sort of reddish/orange/yellow color. I hope the doctor did this properly as I certainly don't want to go through that again. I am concerned there will be a misdiagnosis, but won't think about that now.

The day after, today, it is itchy where the biopsy was done. I want to scratch but it hurts to touch the area. It feels spongy now, whereas before it was more solid and not painful at all. I think the growth has gotten bigger, perhaps because it was invaded and swelled up in reaction. The skin around looks like it has been bruised, but it is more reddish than purplish/blackish. Rather invasive! I wonder if it will be worth it! I asked the doctor how long the results would be. He said 3-4 weeks!!! That is long! I will see him again March 22nd. So meanwhile I will take action and see if I can do a bit more research so I can be better prepared next time!

As for why I would allow this FNA, I felt that I might as well know

if it is cancer or not. Might as well get it out of the way. I compared it to having a lump in my breast. I would rather have this than the surgery. I have had this growth for a long time I admit, started out small then grew bigger as I lost more and more weight over the last year. If it is cancer, I will ask for a second opinion. If it is not cancer, then I will continue on my present course of action which is naturopathy with Tapazole. I should mention I have already gained seven pounds in the last week which is not good news for me! I was overweight before, and was so happy to finally lose weight. To see it come back is distressing and I don't want to starve myself or over-exercise to keep it off.

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TIN

The following study shows that the greatest concentration of tin in the body is in the thymus gland. Since the thymus is a key immune system gland, my suspicion is that tin may somehow be involved in autoimmune diseases such as thyroid diseases.

J Anal Toxicol 1986 Jan-Feb;10(1):6-9

Tin concentration in the thymus glands of rats and mice and its relation to the involution of the gland.

Sherman LR, Masters J, Peterson R, Levine S

Tin is an ubiquitous element and thus enters mammals through the food chain. It has never been found to be dysfunctional in either plants or animal tissue and has been regarded as an innocuous background material. Of the many organs and glands that have been analyzed for tin, only the thymus gland exhibits an above average value for tin. A complete study on the tin content in the thymus gland has never been published and this work is an attempt to investigate this subject. Three types of rodents were used in this study; inbred Lewis rats, inbred A/KI mice (a breast cancer prone mouse) and outbred COBS mice (a cancer resistant mouse). The tin analysis of the muscle, spleen, and thymus indicated constant values for the muscle and spleen tissue, but an increase in the thymic tin concentration (ppm) with age. Besides normal aging studies, the animals were administered the disodium salt of dexamethasone-21-phosphate (dexa), which causes rapid loss of lymphocytes from the spleen and thymus but has no effect upon the muscle. Tin concentration in the muscles remained constant, showed a loss from the spleen and an increase in the thymus gland. The increase indicates that the tin was probably located in the medulla of the thymus, which may be the active biochemical site for tin in rodents. When compared to the COBS mice, the A/KI mice showed a non-statistical difference in tin content in the muscle and spleen and statistically significant lower tin content in the thymus gland.

The following study suggests that tin toxicity can result in psychiatric abnormalities such as psychosis.

G Ital Med Lav Ergon 2000 Jan-Mar;22(1):52-61; discussion 62-3

[Occupational poisoning with psychiatric manifestations].

[Article in Italian]

Candura SM, Butera R, Gandini C, Locatelli C, Tagliani M, Fasola D, Manzo L

Dipartimento di Medicina Preventiva, Universita degli Studi di Pavia.

Numerous occupational intoxications (acute, chronic and their sequelae) may affect the central nervous system and result in a wide variety of neuropsychiatric effects, ranging from subtle behavioural disturbances to overt psychosis. Chemicals causing such manifestations include many metals and organometals (Hg, Mn, Pb, Al, Sn), pesticides (organophosphates), compounds utilised in the industrial setting as solvents or intermediates (carbon disulfide, hydrocarbons and their halogenated derivatives), and combustion products (carbon monoxide). Some types of toxic insults may not be reflected in any clinical manifestation. However, this type of damage may render the brain more vulnerable to additional insult or accelerate physiological loss of neurones with ageing. Thus, occupational exposures to chemicals (Al, Pb, organic solvents) might be involved in the causation of neurodegenerative diseases--such as Alzheimer's disease--which are usually labelled as "idiopathic". A careful occupational anamnesis is crucial to diagnose work-related psychiatric manifestations and--consequently--to interrupt the toxic exposure, to start therapy, and to promote insurance compensation.

Sangyo Eiseigaku Zasshi 1997 Jan;39(1):1-20

t

[Biological activity of tin and immunity].

[Article in Japanese]

Arakawa Y

Department of Hygiene and Preventive Medicine, Faculty of Health Sciences, University of Shizuoka, Japan.

Tin generates a wide variety of biological activities deriving from its chemical character. In this article, the biological activities of tin compounds are reviewed with a focus on the connection with immunity. The table of contents is as follows: Introduction, 1. Inorganic Tin and Immunity, 2. Organic Tin and Immunity, 2.1. Immunotoxicity, 2.1.1. Immunosuppression, 2.1.2. Thymus atrophy, 2.1.3. Changes in the membrane surface

antigens of T cells, 2.2. Antitumor activity, 2.3. Anti-inflammatory action, 2.4. Tolerance manifestation of thymus atrophy, 3. Cellular and Biochemical Aspects of the Activity Manifestation, 3.1. Intracellular distribution of organotins 3.2. Effects on structure and function of Golgi apparatus and endoplasmic reticulum, 3.3. Effects on physical properties of phospholipid membrane, 3.4. Suppressive effects on cell proliferation system, 3.5. Consideration, Conclusion. To sum up this article, tin compounds (especially organotin compounds) act mainly on cellular immune systems and the mechanism appears to be due to their hydrophobicity-dependent intracellular distribution and their action on the phospholipid metabolism including the inhibition of intracellular phospholipid transport between organelles through an impairment of the structure and functions of the Golgi apparatus and the endoplasmic reticulum (ER), and the consequent inhibition of the membrane-mediated signal transduction system leading to DNA synthesis via phospholipid turnover and Ca^{2+} mobilization.

The following study suggests that a tin deficiency might be involved in dental problems.

Int Dent J 1994 Feb;44(1 Suppl 1):107-18

The effect of stannous fluoride on dentinal hypersensitivity.

Thrash WJ, Dodds MW, Jones DL

Department of Community Dentistry, University of Texas Health Science Center at San Antonio 78284-7917.

Many agents have shown varying degrees of effectiveness on pain resulting from exposed dentine. One which has shown some promising results is stannous fluoride (SnF₂). The purpose of the following paper is twofold: to review and summarise the clinical literature pertaining to the relative effectiveness of solutions or gels containing SnF₂ in controlling pain associated with dentinal hypersensitivity; and to statistically re-evaluate these studies in combination, in order to develop recommendations for the optimal use of SnF₂ for hypersensitivity. Seven blinded clinical studies were identified and reviewed. Five of these compared 0.4 per cent SnF₂ gel solution to an identical placebo. One compared a 0.4 per cent SnF₂ gel solution and a 0.717 per cent F solution to an aqueous placebo. The final study compared a 0.717 per cent F solution to an aqueous placebo. Statistical power analysis and a combined meta-analysis were used to ensure adequate internal consistency and to contribute to an overall consensus of the efficacy across time. It was concluded that the 0.717 per cent F solution provides a virtually immediate and definable effect, which seems to continue for several months. This effect was present in all subjects used in the study. This solution was applied directly to the sensitive area for one minute and allowed to remain for 3-5 minutes. An additional one minute application was applied if needed. The effect of the 0.4 per cent SnF₂ gel appears to be more gradual, perhaps involving a different mechanism of action. This solution requires approximately two to four weeks of continuous treatment to be effective. It was concluded that an effective strategy involving the use of stannous fluoride gel includes the application of the 0.717 per cent F solution in the office, effectively providing immediate relief. The patient would then use the 0.4 per cent SnF₂ gel at home in order to achieve the long-term effect. In order to control episodic pain while the gel is developing its effect, a small amount of the 0.717 per cent F solution could be given to the patient for occasional symptomatic application.

J Toxicol Sci 1990 Dec;15 Suppl 4:125-51

The neurotoxicology and pathology of organomercury, organolead, and organotin.

Chang LW

Department of Pathology, University of Arkansas for Medical Sciences, Little Rock 72205.

The toxicities of many metals, such as mercury and lead, are known to man since the dawn of civilization. Organic compounds of some heavy metals are known to have a particular toxic impact on the central nervous system. Organomercury, particularly alkyl-mercuric compounds (e.g. methylmercury), has a selective effect on the granule cells of the cerebellum, the nerve cells of the calcarine cortex, and the sensory neurons in the dorsal root ganglia. The well known Minamata Bay disease is the result of a massive epidemic episode of human exposure to alkylmercury contaminated food sources. Mental retardation and other developmental defects are also known to be a consequence of exposure to this toxic metal. Organic lead compounds have been employed as gasoline additives and in other industrial purposes. Unlike its inorganic counterpart, organolead compounds have a more prominent impact on the central nervous system. Pathological changes of the brain stem neurons have been described. Organotin compounds have been used in plastic industries and as agricultural chemicals. Both trimethyl and triethyl tin compounds are found to be extremely neurotoxic. Despite the similarity of their chemical structures, trimethyl and triethyl tins have a diversely different toxic property and effects. While triethyl tin is myelinotoxic, producing edematous and vacuolar changes in the central myelin, trimethyl tin is neurotoxic, producing prominent toxic changes in the neurons of the limbic system (hippocampus, entorhinal cortex, etc.). The factors which determine the specificity and selectivity of the neurotoxic impacts by various organometals are still unknown. In view that most of the organometals are still widely employed by many countries for industrial and for agricultural purposes, caution must be made for their proper handling and disposal to avoid undesirable exposures to workers and environmental contamination of water sources and food-chain for the common public. Since organometals are difficult to

eliminate from the central nervous system, injuries usually lead to permanent neurological deficits, such tragedies are frequently long lasting and create not only a medical problem, but also a social economical problem for the society.

Thymus 1990 Jun;15(4):223-31

Tin and the thymus gland: a review.

Cardarelli N

Engineering and Science Technology Division, University of Akron, OH 44325.

Experimental studies over the last decade have suggested an association between thymus immune and homeostatic function and exogenous tin. It has been hypothesized that the thymus gland synthesizes and secretes one or more tin bearing factors that enhance immune defenses against malignancy and retard the gradual loss of immune capacity with senescence. This review conciliates data from several divergent areas of research in order to explore the rationale for the above concepts.

Thymus 1988-89;12(2):131-4

Tin in the thymus gland of dogs.

Sherman LR, Cardarelli NF

Department of Chemistry, University of Akron, OH 44325-0001.

The thymus glands from four mixed breed dogs were analyzed to determine the water content, chloroform extractable fraction and residue. The thymi samples were assayed for tin and compared to the tin in the spleen and muscle tissue. The tin content in the thymus gland (29.4 ppm) was higher than the muscle (14.9 ppm) or spleen (12.8 ppm). The tin content in the lipid portion of the thymus was approximately four times greater than the non-chloroform extractable fraction (primarily protein).

Int J Rad Appl Instrum B 1992 Apr;19(3):297-301

m-[125I]iodoaniline: a useful reagent for radiolabeling biotin.

Khawli LA, Kassis AI

Department of Radiology (Nuclear Medicine), Harvard Medical School, Shields Warren Radiation Laboratory, Boston, MA 02115.

Biotinyl-m-[125I]iodoanilide (BIA) was synthesized by coupling biotin to m-[125I]iodoaniline via a mixed anhydride reaction. m-[125I]iodoaniline was produced from the tin precursor, which was prepared using a palladium catalyzed reaction of hexabutylditin with m-bromoaniline. The radioiodinated BIA derivative is characterized by a stable amide and/or intact ureido group on the biotin molecule; it may thus be a useful carrier for targeting radionuclides to avidin-conjugated antibodies previously localized on tumors.

Pharmacology 1996 Mar;52(3):178-86

Effects of a series of metalloporphyrins on adrenal, testicular and thyroid function in rats.

Drummond GS, Smith TJ, Kappas A

Rockefeller University Hospital, New York 10021, USA.

We have extended our earlier studies [Pharmacology 1986;34:9-16] on the effects of certain synthetic heme analogues and cobalt chloride (CoCl₂) on endocrine functions mediated by the hypothalamic-pituitary axis to examine specifically the ability of Sn-protoporphyrin (SnPP) and Sn-mesoporphyrin (SnMP) to perturb adrenal, testicular and thyroid function since there is interest in the use of Sn(tin)-porphyrins in the treatment of hyperbilirubinemia of the newborn. SnPP and SnMP when administered to adult male rats did not alter serum corticosterone, testosterone, thyroxine or triiodothyronine levels when compared to control animals. In addition, administration of exogenous adrenocorticotrophic hormone produced an increase in serum corticosterone levels that was comparable in placebo-treated and SnPP- and SnMP-treated animals. These studies involved doses of both compounds substantially greater than those used clinically. The results clearly indicate that SnMP, presently the compound of choice for use in newborns, and SnPP do not in the doses studied impair adrenal, testicular and thyroid function in vivo.

Chronic toxicity and carcinogenicity of bis(tri-n-butyltin)oxide (TBTO) in the rat.

Wester PW, Krajnc EI, van Leeuwen FX, Loeber JG, van der Heijden CA, Vaessen HA, Helleman PW

National Institute of Public Health and Environmental Protection, Bilthoven, The Netherlands.

In a 106-wk toxicity and carcinogenicity study, groups of 60 male and 60 female weanling Wistar rats were fed 0, 0.5, or 50 mg bis(tri-n-butyltin)oxide (TBTO)/kg diet. In males, feed consumption was increased in all treated groups and increased water consumption occurred at 5 and 50 mg/kg. During the second year, body weight decreased in the 50-mg/kg males, while the females in that group showed no weight gain. Excess mortality was confined to the 50-mg/kg group towards the end of the study. Haematological changes, comprising anaemia, lymphocytopenia and thrombocytosis were noted mainly at the high-dose level. Also, signs of decreased kidney function and increased plasma enzyme activities (alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase) were noted. No effects on serum hormone concentrations (thyrotropin, follicle stimulating hormone, luteinizing hormone or insulin) were observed, except for a decrease in the free thyroxine:thyroxine ratio in both sexes at the high-dose level. Higher serum IgM and IgA levels were present at 50 mg/kg, while, in females, IgG was decreased. At 50 mg/kg, the ovaries, adrenals, spleen (females), heart (males), pituitary, liver and kidneys were increased in weight, but the thyroid weight was decreased in females. The total tin concentrations in liver and kidneys showed a dose relationship and, in general, the concentrations were similar after 1 and 2 yr. Non-neoplastic histological alterations after 1 yr consisted of a decrease in the cell height of the thyroid follicles in all dose groups, with a reduced number of psammoma bodies at 50 mg/kg, a decrease in splenic iron content at 5 (females only) and 50 mg/kg, and a slight bile-duct activation. After 2 yr, only the thyroid changes were still present. In addition, at 2 yr, vacuolation and pigmentation of the proximal tubular epithelium and nephrosis were enhanced at 50 mg/kg. The incidence of benign tumours of the pituitary was significantly elevated and enhanced at 0.5 and 50 mg/kg. At 50 mg/kg increases in pheochromocytomas in the adrenal medulla and in parathyroid adenomas (males) were noted, while adrenal cortical tumours were decreased (males). There was a low, non-dose-related incidence of pancreatic carcinoma. Other tumour rates were in line with control data. It is concluded that lifetime feeding of 50 mg TBTO/kg diet induces toxicity in various organ systems. An increase in some common tumours was found at the high dose, probably due to hormonal or immunological changes.

Radiology 1977 Aug;124(2):445-50

The effect of tin on the tissue distribution of ^{99m}Tc-sodium pertechnetate.

Ancrì D, Lonchamp MF, Basset JY

When tin complex is administered prior to the injection of ^{99m}Tc-sodium pertechnetate, the distribution of the tracer is altered such that: (a) the concentration at foci of cerebral pathology is drastically reduced; (b) the concentration in the stomach (mucus cells), thyroid and salivary glands, and choroid plexus is greatly increased; and (c) there is a shift of the tracer from the plasma to the red blood cells. Bone studies utilizing a tin complex should be done after other organs have been evaluated.

:Arch Toxicol 1981 Jul;47(4):263-8

[inkOut](#)

Distribution of tin in the rat and disturbances in the metabolism of zinc and copper due to repeated exposure to SnCl₂.

Chmielnicka J, Szymanska JA, Sniec J

The effect of stannous chloride on tissue concentrations of zinc and copper was studied in female rats. The animals were subjected to repeated exposure to seven doses given every other day 2 mg Sn/kg, subcutaneously. About 60% of tin ¹¹³Sn was retained in the body. Of this amount, about 95% accumulated in the skin and hair. In the remaining organs the tin concentrations corresponded to 2.57 to 0.0001% of the retained dose. In comparison with the control group a 3-fold increase of the content of zinc was found in the liver while a decrease was revealed in the spleen, heart, brain, lungs, and especially in muscle. A statistically significant decrease of the copper content was found in the blood and brain.

The following study indicates a connection between tin and lithium.

Org Lett 2000 Jun 1;2(11):1561-4

Synthesis and reactivity of conformationally locked alpha-aminoorganostannanes and alpha-aminoorganolithiums. Discovery Of a surprising configurational requirement for transmetalation.

Chambournier G, Gawley RE

Department of Chemistry, University of Miami, P.O. Box 249118, Coral Gables, Florida 33124, USA.

[Medline record in process]

2-Tributylstannyl-N-methylpiperidines that are conformationally locked by a 4-tert-butyl substituent were evaluated in transmetalations (Sn-Li exchange) and reactions with electrophiles. When the tin is equatorial, transmetalation occurs smoothly as does reaction with carbonyl electrophiles. Alkyl halides seem to undergo single electron transfer reactions, affording nonselective alkylation products, along with products of radical disproportionation. In a surprise, an axially oriented tin failed to transmetalate, suggesting that a synclinal relationship between the nitrogen lone pair and the carbon-tin bond is a requirement for transmetalation.

J Immunol 1989 Dec 15;143(12):3981-7

Immune stimulatory properties of metalloporphyrins.

Novogrodsky A, Suthanthiran M, Stenzel KH

Rogosin Institute, Cornell University Medical College, New York 10021.

A possible approach to the immunotherapy of tumors is to stimulate either specific or nonspecific immune responses in vivo. We recently found that provision of a mitogenic signal to PBMC, by incubation with the oxidizing mitogens, enhanced the effect of IL-2 in generating cytolytic activity. We therefore searched for a mitogen that might safely be administered to patients. The present study is an investigation of the mitogenic properties of iron and tin (Sn)-protoporphyrin and their capacity to induce cytotoxicity in human PBMC. These agents have been administered to humans with little toxicity. Both iron- (hemin) and Sn-protoporphyrin induce mitogenicity in peripheral T cells. This effect is markedly enhanced by low concentrations of IL-2. Hemin and Sn-protoporphyrin, in combination with IL-2, increase IL-2R on PBMC. Hemin alone, and to a greater extent in combination with IL-2, induces cytotoxicity for NK-sensitive and NK-resistant cell lines. Sn-protoporphyrin, a more potent mitogen than hemin, fails to induce cytotoxicity, and has a marked inhibitory effect on cytotoxicity induced by IL-2. Hemin and Sn-protoporphyrin stimulate TNF-alpha and IFN-gamma production by PBMC. IL-2 is synergistic with the metalloporphyrins in eliciting this effect. Metalloporphyrin-induced mitogenesis has a stringent requirement for macrophages. Scavengers of oxygen-free radicals and inhibitors of peroxidase inhibit mitogenicity induced by hemin but not that induced by Sn-protoporphyrin. Hence, an oxidative event may mediate the mitogenic effect of hemin. Our results indicate that hemin is an immunostimulatory agent in vitro and the data warrant further evaluation of its in vivo immunostimulatory and antitumor effect.

Aust J Exp Biol Med Sci 1984 Apr;62 (Pt 2):199-208

Organotin implications in anticarcinogenesis. Background and thymus involvement.

Cardarelli NF, Quitter BM, Allen A, Dobbins E, Libby EP, Hager P, Sherman LR

A comprehensive study of the scientific literature regarding tin content in normal and pathogenic human tissue has disclosed that various organotin materials retard both the onset and growth of cancer in laboratory animals, and decreased tissue tin in humans may be associated with tumour development. Initial studies by the authors have shown that the thymus gland of the mouse possesses a relatively high concentration of tin and is also the major site of accumulation for ¹⁴C-labelled tri-n-butyltin fluoride (TBTF). When mammary cancer-prone mice with transplanted tumours were orally dosed continuously with this agent in their drinking water, the tumour growth rate was significantly reduced. Both mouse mammary tumours and human lung tumours show low tin content compared to normal body tissue.

The following study seems to suggest that tin (in combination with vinyl) can facilitate the synthesis of estradiol. Since there is some evidence that food from tin cans might be a facilitator of hyperthyroidism, at least in cats, there might be some connection between tin from cans, and an increase in estradiol (which seems to increase cadmium uptake). Also there is mention of selenium-estradiol compounds, which I'd like to investigate further.

Steroids 1996 Jun;61(6):384-9

Synthesis and estrogen receptor binding of (17 alpha, 20E)- and (17 alpha, 20Z)-21-phenylthio- and 21-phenylseleno-19-norpregna-1,3,5(10),20-tetraene-3,17 beta-diols.

Napolitano E, Fiaschi R, Herman LW, Hanson RN

Department of Pharmaceutical Sciences, Bouve College of Pharmacy and Health Sciences, Northeastern

Previous studies from our laboratory using 17 α -E- and 17 α -Z-halovinyl estradiols demonstrated a marked enhancement of receptor binding by the Z-isomers. This suggested tolerance at the 17 α -position was not previously observed by investigations using 16 α and 17 α -substituted estradiols. **Because of the synthetic access provided by vinyl tin chemistry**, we prepared the 17 α -E and Z-phenylthiovinyl and phenylselenovinyl estradiols and compared their binding characteristics to those of the previously reported 16 α /17 α -phenylseleno and methylseleno estradiols. The results, in addition to demonstrating a facile preparation of the target compounds, indicated that significant receptor affinity was retained by these compounds (relative binding affinity = 24.5-117). The highest affinity was demonstrated by the 17 α -Z-phenylthiovinyl estradiol 5a, which, by molecular modeling, exhibited a significantly different molecular conformation from the corresponding 17 α -E-phenylthiovinyl isomer or the 17 α -phenyl-thioethynyl analog. The current series possessed better binding characteristics than the phenylseleno and methylseleno estradiols but somewhat poorer binding than the 17 α -E/Z-halovinyl series. The observations suggest that some steric limitations exist in a portion of the 17 α -region, and that the region is better accessed by compounds possessing Z-vinyl stereochemistry.

J Steroid Biochem Mol Biol 1993 Nov;46(5):613-22

Synthesis, receptor binding and biodistribution of the gem-21-chloro-21-iodovinylestradiol derivatives.

Ali H, Rousseau J, van Lier JE

MRC Group in the Radiation Sciences, Faculty of Medicine, University of Sherbrooke, Quebec, Canada.

Radioiodinated 11 beta-methoxy-(17 α ,20E)iodovinylestradiol (11 beta-OMe-IVE2) shows high estrogen receptor (ER)-mediated uterus uptake and good potential as an ER-imaging agent. In order to examine the tolerance of the ER for modification about the iodovinyl substituent, we prepared the (17 α ,20Z-chloro)21-chloro-21-iodovinylestradiol (4a) and several derivatives featuring 11 beta-methoxy (4b), 11 beta-ethoxy (4c) or 7 α -methyl (4d) substituents. All gem-dihalogen derivatives 4a-d were prepared from the 17 α -chloroethynyl precursors. The intermediate chlorostannylvinyl derivatives were obtained using tri-n-butyltin hydride and palladium acetate catalyst. Compounds 4a and 4b were labeled with ¹²⁵I via their corresponding tin intermediates and their tissue distribution was studied in immature female rats. Addition of a 21-Cl to the 17 α -ethynylestradiols reduced ER binding affinity, except for the 11 beta-substituted analogs which showed a pronounced increase. Surprisingly, addition of a 21-Cl to the (17 α ,20E)IVE2 resulted in increased ER binding affinities and augmented ER-mediated uterus uptake, which may result from the pronounced increase in the dipole moment of the molecule. Thus, further modifications at the C-21 position of IVE2 are well tolerated by the ER. However, addition of the 21-Cl also resulted in increased radioiodine uptake by the thyroid, much slower blood clearance and lower uterus to blood/nontarget ratios, suggesting increased in vivo instability of the C--I bond of the gem-chlorine-iodine atoms which may reflect the increase in steric and electronic interference.

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TYRAMINES

Tyramines are amino acid products which are associated with headaches and hypertension. Tyramines may be produced from the amino acids phenylalanine and tyrosine. Tyrosine is the amino acid which is used by the body to form thyroid and catecholamine (epinephrine, norepinephrine, etc.) hormones.

Tyramines are found in high amounts in certain foods such as chocolate, wine, beer, cheese, beans, liver, and other foods (list below). These are the foods which are associated with migraine and other headaches in certain individuals, especially women.

Tyramines appear to be broken down in the body by an enzyme called monoamine oxidase (MAO). Apparently monoamine oxidase is also the same enzyme that breaks down the thyroid and catecholamine hormones after their use is finished and to prevent an excess of these hormones from circulating throughout the body. When there is an excess of the catecholamines in circulation, a condition of hypertension may result. When there is an excess of thyroid hormones in circulation, hyperthyroidism results.

What makes monoamine oxidase particularly important in the study of the cause of thyroid disease, is that MAO is a copper containing enzyme. We have seen that a deficiency of copper is probably the major cause of hyperthyroidism. An excess of copper or copper unbalanced by other minerals may lead to depression and possibly hypothyroidism.

It's possible that the reason copper is so important to thyroid status is its role in forming MAO. Possibly a deficiency of MAO leads to excess thyroid and catecholamine hormones, hypertension, the perception of being stressed, and hyperthyroidism. An excess of MAO may deplete the body of the thyroid and catecholamine hormones leading to hypothyroidism and depression.

One study looked at MAO levels in hyperthyroid patients and found that MAO levels are low. The authors speculated that low MAO may be involved in hyperthyroidism. (See [MAO and MAOI](#))

There is a class of antidepressants known as monoamine oxidase inhibitors (MAOI) which are prescribed for depressed individuals. These MAOI deplete the body of excess MAO allowing a normal amount of catecholamines and 5-HT to circulate which relieves depression.

When all this information is put together there is good reason to believe that the tyramines adversely affect persons who are low in copper, because copper is necessary for the production of MAO which is needed to break down the tyramines. In these individuals, the tyramines may increase the drain on MAO and copper and thereby increase the symptoms associated with low copper: headaches, hypertension, and hyperthyroidism.

Check out the list of high tyramine foods to see if these foods create problems for you. If these foods bother you, then you may be deficient in copper. Some of these foods we have listed as high copper foods, such as chocolate, beer, nuts, and beans. It may be possible that foods like chocolate and beer, while they contain copper, may use up more copper than they provide because of the drain of MAO.

HIGH TYRAMINE FOODS

Chocolate
Beer, ale, and wine
Aged and cultured dairy products (cheese, yogurt, etc.)
Banana
Nuts
Beans and legumes
Liver
Figs, prunes, raisins, pineapple (possibly only canned)
Soy sauce and MSG
Vanilla
Yeast
Pickled and salted fish

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VANADIUM

Rough file:

"When Dr. John McNeill, dean of pharmaceutical sciences at UBC, and his colleagues Clayton Heilinger and Arun Tahiliani were testing vanadium - a common trace element found in seaweed - on diabetes induced female rats to see if it would prevent the development of cardiac problems, they made a startling discovery. Vanadium not only improved the rats' cardiovascular performance, it also regulated the levels of glucose in their blood and prevented the formation of cataracts. In fact, the rats that were fed vanadium in their drinking water appeared normal in all respects. ... Adds McNeill: 'The fact that vanadium appears to fix the whole system is a very nice discovery. It was not something we originally intended to look for.'

On average, an adult consumes one to four milligrams of vanadium every day from such foods as meat, milk, vegetables and bread: fish and marine plants are particularly good sources. The biological importance of vanadium, however, is largely unknown. A natural part of the regulatory system, it is believed to prevent cholesterol formation both in blood vessels and in the central nervous system. ... However, says McNeill, 'we never thought vanadium would do it [mimic insulin] so well. From everything we looked at, the rats were completely normal.'

A two-factor, two-by-three factorially arranged experiment was performed to ascertain whether iodine affects the response of rats to vanadium deprivation. Male weanling Wistar-Kyoto rats were fed a 16% casein 68% acid-washed ground corn diet for 8 weeks. The variables were supplemental vanadium at 0 or 1 microgram/g and supplemental iodine at 0, 0.33 or 25 micrograms/g. Vanadium deprivation increased thyroid weight and thyroid weight/body weight ratio and decreased the concentration of vanadium in liver. Vanadium and iodine interacted such that, as dietary iodine was increased, plasma glucose increased in the vanadium-deficient rats but decreased in the vanadium-supplemented rats. Also, as dietary iodine was increased, thyroid peroxidase activity decreased; the decrease was more marked in the vanadium-supplemented than the vanadium-deprived rats. The findings suggest that vanadium may have a physiological role affecting iodine metabolism and thyroid function. [vanadium and iodine interaction effects on thyroid.doc](#)

The following study shows that vanadium supplementation can increase bone mineral levels and that there is an interaction between vanadium and vitamin C in cholesterol metabolism.

Magnes Trace Elem 1991-92;10(5-6):327-38

Vanadium and ascorbate effects on 3-hydroxy-3-methylglutaryl coenzyme A reductase, cholesterol and tissue minerals in guinea pigs fed low-chromium diets.

Seaborn CD, Mitchell ED, Stoecker BJ

Department of Nutritional Sciences, Oklahoma State University, Stillwater.

Vanadium has been reported to affect numerous physiological processes; however, a demonstration that vanadium deficiency consistently impairs biological function is lacking. The purpose of this study was to determine if the activity of hepatic 3-hydroxy-3-methylglutaryl coenzyme A (HMG CoA) reductase, the rate-limiting enzyme in cholesterol synthesis, is affected by dietary supplementation of vanadate and/or chronic ascorbic acid deficiency. To determine if vanadium and/or ascorbic acid affected mineral metabolism, tissue minerals also were analyzed. Weanling male guinea pigs were assigned randomly to groups of 10 in a 2 x 2 factorial design. The dietary variables were ascorbate, 0.5 or 10 mg/day, and vanadium < 0.01 microgram or 0.5 microgram/g diet as NH₄VO₃ in a low Cr diet containing < 0.07 microgram Cr/g diet. After 21 weeks on this diet, guinea pigs receiving more ascorbate had lower liver weight/body weight ratios and increased bone copper. Testes weight/body weight ratios, hepatic glycogen and bone copper decreased while hepatic lipids, fecal bile acids, plasma cortisol and bone calcium and magnesium were increased by vanadium supplementation. An interaction between vanadium and ascorbate affected cholesterol excretion in feces, hepatic iron, plasma cholesterol concentration and the activity of HMG CoA reductase. **This study provides evidence of increased bone mineral concentrations with vanadium supplementation and of an interaction between vanadium and ascorbate which affected cholesterol metabolism.**

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VITAMIN A

Vitamin A deficiency has been shown to increase T3 and this is further increased by an additional deficiency of iodine. "In the A- and A-I- groups, blood levels of retinol fell to one tenth of the control mean and circulating concentrations of total and free T4 and T3 increased significantly. This biochemical hyperthyroidism contrasted with the maintenance of normal TSH plasma values, suggesting a generalized peripheral refractoriness to thyroid hormones." [vitamin A deficiency causes hyperT.doc](#)

The conversion of beta carotene into vitamin A is driven by thyroid hormone. In hyperthyroidism, beta carotene is converted rapidly into vitamin A (which I believe indicates a deficiency of A), while in hypothyroidism, beta carotene conversion to A is markedly decreased, resulting sometimes in a yellowish tint to the skin of a hypo who is consuming beta carotene rich foods. JJ

The following study shows that copper deficiency results in higher liver concentrations of vitamin A (retinol) and lower blood levels of vitamin A, suggesting that "a copper-deficient diet may cause defective transport of vitamin A from liver to blood."

Title

Modification of vitamin A metabolism in rats fed a *copper*-deficient diet.

Author

Rachman F; Conjat F; Carreau JP; Bleiberg-Daniel F; Amedee-Manesme O

Address

INSERM U 56, Universit'e Paris-Sud, H'opital d'Enfants, Bic'etre, France.

Source

Int J Vitam Nutr Res, 57(3):247-52 1987

Abstract

The liver is the main storage site of vitamin A and *copper*. Inverse relationships between *copper* and vitamin A liver concentrations have been suggested. We have investigated the consequences of a *copper*-deficient diet on liver and blood vitamin A storage in Wistar rats. Animals were fed either a *copper*-deficient diet for 45 days from weaning, or an identical diet containing adequate amounts of *copper*. Concentrations of vitamin A were determined by isocratic high performance liquid chromatography using UV detection. We have observed in the liver of the rats fed a *copper*-deficient diet a significantly higher mean level of retinyl esters (148 +/- 37 micrograms/g of liver) and retinol (3.3 +/- 1.4 micrograms/g of liver) compared to the mean concentration of the retinyl esters (53 +/- 8.5 micrograms/g of liver) (p less than 0.01) and retinol (1.4 +/- 0.5 micrograms/g of liver) (p less than 0.01) in controls. Opposite results were observed in the serum of the group fed a *copper*-deficient diet as these rats had a significantly lower level of retinol (22 +/- 4 micrograms/100 ml) compared to the mean concentration in the controls (64 +/- 20 micrograms/100 ml) (p less than 0.01). These findings suggest that a *copper*-deficient diet may cause defective transport of vitamin A from liver to blood. This experimental model may be useful to further investigate unusual liver vitamin A and *copper* concentrations observed in children during various hepatobiliary diseases.

Title

[Beta-carotene, vitamin A and carrier proteins in thyroid diseases]

Author

Aktuna D; Buchinger W; Langsteger W; Meister E; Sternad H; Lorenz O; Eber O

Address

Internen Abteilung, Krankenhauses der Barmherzigen Br"uder Graz-Eggenberg.

Source

Acta Med Austriaca, 20(1-2):17-20 1993

Abstract

The conversion of beta-carotene (provitamin A) to 2 molecules of vitamin A (retinol) is accelerated by thyroxine and hyperthyroidism, respectively. The characteristic yellow tint of the skin in hypothyroidism is due to hyper-beta-carotenemia. Both in hyper- and hypothyroidism a retinol deficiency has been observed in literature. In a series of 36 patients (16 hyper-, 8 hypo-, and 12 euthyroid) serum samples were analyzed for retinol and beta-carotene levels (high pressure liquid chromatography) as well as retinol binding protein (radial immune diffusion), prealbumin (nephelometry), and serum *zinc* values (atomic absorption spectrometry) were established. The beta-carotene serum level in the hypothyroid group (mean 1.1 microgram/ml) was significantly higher (p < 0.05) in relation to euthyroid controls (0.6 microgram/ml), the hyperthyroid group showed significantly lower values (0.3 microgram/ml). RBP and prealbumin concentrations were significantly lower (p < 0.05) in hyperthyroid as against eu- and hypothyroid patients. Surprisingly, in all 3 groups the retinol levels were not significantly different, although the hyperthyroid group was slightly lower (0.6 microgram/ml) than the mean value of 0.7 micrograms/ml in the other groups. A vitamin A and protein rich food, customary in Central Europe, seems to rule out any vitamin A deficiency both in hyper- and hypothyroidism. However, the beta-carotene values are significantly higher in hypothyroidism, while in hyperthyroidism they were lower. As intrahepatic *zinc* content plays an important role in the synthesis of RBP and its secretion together with retinol, we also analyzed this component: The serum *zinc* levels in hyperthyroid patients were clearly higher (79.1 micrograms/dl) than in the hypothyroid group with 57 micrograms/dl (p < 0.05).

The following study indicates that hyperthyroid cats have a 30% high level of vitamin A (retinol) and a 30% lower level of vitamin E (alpha-tocopherol) than normal cats.

Am J Vet Res 1993 Apr;54(4):563-9

Comparison of taurine, alpha-tocopherol, retinol, selenium, and total triglycerides and cholesterol

concentrations in cats with cardiac disease and in healthy cats.

Fox PR, Trautwein EA, Hayes KC, Bond BR, Sisson DD, Moise NS

Department of Medicine, Animal Medical Center, New York, NY 10021.

Epidemiologic relations were evaluated between plasma concentrations of nutrients and cardiovascular diseases. A total of 220 cats were assessed: 144 cats with noninduced acquired heart disease and 76 clinically normal cats. Plasma was assayed for taurine, alpha-tocopherol, selenium, retinol, and total cholesterol and triglycerides concentrations. Cardiovascular disease groups included dilated cardiomyopathy (n = 53), left ventricular hypertrophy (n = 28), hyperthyroidism (n = 11), and uncertain classification (n = 52). In cats with dilated cardiomyopathy, mean plasma taurine concentration was the lowest of that in cats of any group, being only 38% of the value in healthy cats; females had less than half the mean value of males. Tocopherol concentration was 20% lower than normal, and retinol concentration was 40% higher than normal. Total cholesterol concentration was 36% lower than normal. Triglycerides concentration was higher in these cats than in any other group--twice the value recorded in healthy cats and 67% higher than that in hyperthyroid cats. In cats with hypertrophic cardiomyopathy, almost 15% had mean plasma taurine concentration < 30 $\mu\text{mol/L}$. Retinol concentration was 15% higher, and triglycerides concentration was 54% higher than normal. Approximately 27% of hyperthyroid cats had mildly decreased plasma taurine concentration. Hyperthyroid cats had the lowest tocopherol and cholesterol values; both were at least 30% lower than normal. Retinol concentration was 30% higher than normal. Approximately 14% of cats with uncertain classification had mildly decreased plasma taurine concentration. Plasma retinol and triglycerides concentrations were higher than normal in 25 and 38% of these cats, respectively.

Acta Med Austriaca 1983;10(2-3):71-3

[t](#)

[Vitamin A and carotene in thyroid diseases].

[Article in German]

Smolle J, Wawschinek O, Hayn H, Eber O

From 190 goitrous patients (106 euthyroid, 53 hyperthyroid, 31 hypothyroid) serum levels of vitamin A and carotene were obtained. The serum levels of vitamin A were significantly decreased in both hyperthyroidism and hypothyroidism, the serum levels of carotene in hypothyroidism only. Remarkably, vitamin A levels almost never drop to subnormal values in hyperthyroidism. There is evidence, that a sufficient dietary protein supply enables the liver cell to produce enough amounts of retinol binding protein and prealbumin to overcome the increased clearance observed in hyperthyroid conditions.

Experientia Suppl 1983;44:264-97

Vitamin A-deficiency impairs the normal mannosylation, conformation and iodination of thyroglobulin: a new etiologic approach to endemic goitre.

Ingenbleek Y

This study was undertaken in order to validate the hypothesis that vitamin A-deficiency alters the structure of thyroglobulin (Tg). For that purpose, four groups of 20 Sprague-Dawley rats were submitted during two months to varying dietary conditions, namely a control diet (C+), a vitamin A-deficient diet (A-), an iodine-deficient diet (I-) and a diet characterized by the association of both deficiencies (A-I-). Both the conventional parameters of thyroid function, the intracellular steps of Tg glycosylation and iodination were analyzed. In the A- and A-I- groups, blood levels of retinol fell to one tenth of the control mean and circulating concentrations of total and free T4 and T3 increased significantly. This biochemical hyperthyroidism contrasted with the maintenance of normal TSH plasma values, suggesting a generalized peripheral refractoriness to thyroid hormones. In both A- and A-I- groups, thyroid cytosol 3H-RPM (retinyl-phosphate-mannose) and 3H-mannose incorporation into the core of the 12S-Tg and 19S-Tg species were reduced by 40-50%. In contrast, cytosolic concentrations of 3H-DPM (dolichyl-phosphate-mannose) rose, suggesting that the N-glycosylation pathways are affected in opposite direction. The sedimentation coefficient in sucrose gradient of the purified dimeric 125I-19S-Tg after guanidine 6M and dithiothreitol denaturation showed that most of the A- Tg molecules were transformed into monomeric 12S species, implying alterations of both noncovalent and covalent bonds. Finally, the radiochromatogram of 125I-iodothyronines recovered after Tg pronase digestion revealed a significant increase in the mono- (MIT) and diiodothyronine (DIT) fractions in contrast with a significant decrease in the T3 and T4 hormonal compounds. These findings are consistent with the view that vitamin A-depletion impairs the endogenous RPM synthesis and, therefore, the normal Tg O-mannosylation. The growing peptide is characterized by steric hindrance, leading to abnormal closure of disulphide bonds, reduced MIT-DIT coupling reactions and depressed generation of physiologically active thyroid hormones. pure iodine deficit (I-) induces no effects on the above-mentioned glycosylation reactions, but iodine shortage superimposed on preexisting vitamin A-deficit (A-I-) aggravates the Tg dysmaturation

The following study indicates that the benefits of vitamin A supplementation on the hyperthyroid state has been "described for a long time."

Retinoic acid decreases retinoic acid and triiodothyronine nuclear receptor expression in the liver of hyperthyroidic rats.

Higueret P, Pallet V, Coustaut M, Audouin I, Begueret J, Garcin H

Laboratoire de Nutrition, ISTAB, Universite Bordeaux I, Talence, France.

Retinoic acid (RA) and triiodothyronine (T3) exert many of their actions by binding to specific nuclear receptors (respectively, RA receptor (RAR) and T3) receptor (TR) belonging to a 'superfamily' of receptors. Some heterologous regulation of these receptors has been shown, and in particular regulation of the maximum binding capacity of TR by either retinol or RA. Now, using hyperthyroidic rats as a model, the effect of RA on binding capacity and on the mRNA levels of TR and RAR was investigated. The results show that the benefit of vitamin A treatment for the hyperthyroidic state, which has been described for a long time, could be the result of a down-heteroregulation of TR by RA, the active metabolite of retinol.

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VITAMIN B-12

Vitamin B-12 is the cobalt-containing vitamin and levels can be judged by cobalt levels in the hair analysis. B-12 is critical for iron metabolism and a deficiency of B-12 will lead to anemia and probable hypothyroidism.

If you are hypo and supplementation with iron causes a problem, then suspect either a B-12 deficiency or a copper deficiency. If you are hyper and B-12 causes an increase in hyper symptoms, then suspect a copper deficiency (because B-12 will push iron metabolism and thereby suppress copper).

B-12 deficiency is very likely in persons with hypothyroidism and persons who have been taking copper and iron to recover from hyperthyroidism. Supplementation with high amounts of the other B vitamins, iron, and possibly manganese may use up B-12 creating a deficiency. This may be detected by experiencing adverse reactions to copper, iron, manganese, B vitamins, and many foods.

It is easy to determine a B-12 deficiency by taking a large dose (5000 mcg) since B-12 will have noticeable effects within several hours in a person who is deficient. If you are hypo, feel tingling in the hands, feet, or face, have a low pulse rate, feel your heart beating hard but not excessively rapid at night, or have adverse effects to iron, copper, or zinc, then try some B-12. If you are hyper and just commencing supplementation of copper and other supplements, do not take B-12. You may need to take some later as your hyper symptoms subside and you begin iron supplementation, but avoid it at the beginning.

Find an enteric coated 5000 mcg B-12 tablet. B-12 is destroyed by stomach acid so the enteric coating preserves it until it reaches the intestines where it can be absorbed. The sublingual types of B-12 apparently do not contribute a significant amount of B-12 to the body, but will provide a small but quicker energy boost.

Studies:

This powerful vitamin is essential for those who are strict vegetarians or those with nervous complaints. It is a great energiser of the nervous system and can reduce depression and fatigue. It is required for phase one detoxification of chemicals in the liver, and can help people who are allergic to sulphites, which are common food and wine additives. A study showed that vitamin B12 can effectively block most of the adverse reactions to sulphites such as hay fever, sinus, headache and bronchial spasms. B12 is required in increased amounts by those who use alcohol excessively or in liver disease.

Metal-free, zinc, copper, and rhodium analogues of vitamin B12 were synthesized to further characterize structural requirements for the binding to human intrinsic factor, transcobalamin I, and transcobalamin II. Binding affinities of the various analogues were studied by competition against cyano[57Co]cobalamin. When albumin-coated charcoal was used for the separation of free and bound corrinoids, the relative 50% inhibition indexes were determined. The influence of metal substitution was similar among the three binding proteins. For analogues with a strong coordinative linkage between the heterocyclic base and the central metal ion, similar to that with cobalt (e.g., zinccobalamin and cyanorhodibalamin), the indexes range from 0.65 to 2.35 for all three binding proteins. Analogues in which coordination is impossible (hydrogenobalamin and dicyanorhodibalamin) exhibit markedly reduced binding with indexes between 10 and 160. Cupribalamin shows 50% inhibition indexes ranging from 2.3 to 5.0, thus suggesting a weak coordinative bond between the copper ion and the 5,6-dimethylbenzimidazole moiety. These results emphasize the importance of the coordinative linkage between the central metal ion and the nucleotide moiety for optimal recognition by vitamin B12 binding proteins. [vitamin B12 analogues of cu, zn, rh.doc](#)

The following study shows that pectin can rapidly decrease body levels of B-12. Pectin is found in fruit.

J Nutr 1988 Dec;118(12):1495-501

Effect of hypothyroidism on methylmalonate excretion and hepatic vitamin B-12 levels in rats.

Stokstad EL, Nair CP

Department of Nutritional Sciences, University of California, Berkeley 94720.

The effect of hypo- and hyperthyroidism on vitamin B-12 metabolism in the rat was studied by measuring methylmalonic acid excretion, B-12 content of liver and oxidation of 2-[14C]histidine. Ten percent pectin was added to increase severity of B-12 deficiency. The addition of thiouracil to a diet containing 10% pectin decreased the excretion of methylmalonic acid suggesting an amelioration of the B-12 deficiency. It was found that part of this decreased methylmalonic acid excretion was due to a decreased food consumption with a correspondingly decreased intake of branched-chain amino acids which are precursors of methylmalonic acid. When attempts were made to increase the protein intake of animals receiving thiouracil so their amino acid intake was equal to that of the control animals, methylmalonic acid excretion was still lower than that of the controls. It was also found that the vitamin B-12 content of the liver was higher in the animals receiving thiouracil than in the controls. Thyroidectomy had the same effect as feeding thiouracil. Liver B-12 levels are rapidly depleted on a B-12 deficient diet containing 10% pectin. It appears that hypothyroidism, induced either by thyroidectomy or by feeding thiouracil, slows the rate of depletion of hepatic B-12 which in turn facilitates the metabolism of methylmalonic acid and decreases its excretion in the urine.

Annu Rev Nutr 1985;5:115-41

Vitamin B12-folate interrelationships.

Shane B, Stokstad EL

The studies discussed in this review support the view that biochemical and clinical symptoms common to both folate and vitamin B12 deficiency are due to the induction of a functional folate deficiency, which in turn is induced by cobalamin deprivation. The interrelationship between these two vitamins is best explained by the methyl trap hypothesis stating that vitamin B12 deficiency can lead to lowered levels of methionine synthetase, which results in a functional folate deficiency by trapping an increased proportion of folate as the 5-methyl derivative. In addition, as 5-methyl-H4PteGlu is a poor substrate for folylpolyglutamate synthetase, there is a decreased synthesis of folylpolyglutamates and consequently a decreased retention of folates by tissues. The real folate deficiency that ensues because of decreased tissue folate levels is probably as important physiologically as the functional deficiency caused by the methyl trap. The sparing effect of methionine can be explained by adenosylmethionine inhibition of methylenetetrahydrofolate reductase, which would prevent the buildup of 5-methyl-H4PteGlu. A deficiency in vitamin B12 would not, in itself, be sufficient to cause a disturbance in folate metabolism. The deficiency would have to result in lowered methyltransferase levels before any such disturbance would be manifest.

Nuklearmedizin 1979;18(6):278-82

Serum vitamin B12 and folic acid levels in hyperthyroidism.

Gyftaki H, Kesse-Elias M, Koutras D, Pandos P, Papazoglou S, Mouloupoulos S

Serum vitamin B12 and folic acid levels were measured in 48 hyperthyroid patients and in a group of euthyroid controls. The levels of vitamin B12 ranged from 120-900 pg/ml with a mean of 429.3 +/- 30.9 pg/ml (SE). The mean serum vitamin B12 level was lower in hyperthyroid patients than in normal controls, the difference being statistically significant ($t = 2.584$, p less than 0.025). Serum vitamin B12 levels showed a statistically significant negative correlation with the clinical index of Grooks et al. ($r = 0.344$, p less than 0.05). The findings, although not excluding the involvement of auto-immune gastritis in patients with low serum vitamin B12 levels, suggest a direct action of increased thyroid hormone concentrations. Serum folic acid levels ranged from 0.5-13.8 ng/ml with a mean of 6.8 +/- 0.46 ng/ml (SE). The mean serum folic acid levels were higher in the hyperthyroid patients than in normal controls but the difference was not statistically significant ($t = 1.2$, p greater than 0.2). The serum folic acid levels did not show any statistically significant correlation with the clinical index of Grooks et al. The fact that no statistically significant difference was found between the mean value in hyperthyroid patients and the mean value in normal controls is probably due to the high folic acid intake in Greece.

Brain Res 1996 Jul 15;727(1-2):31-9

Vitamin B12 affects non-photic entrainment of circadian locomotor activity rhythms in mice.

Ebihara S, Mano N, Kurono N, Komuro G, Yoshimura T

Department of Animal Physiology, School of Agricultural Sciences, Nagoya University, Japan.

Administration of vitamin B12 (VB12) has been reported to normalize human sleep-wake rhythm disorders such as non-24-h sleep-wake syndrome (HNS), delayed sleep phase syndrome (DSPS) or insomnia. However, the mechanisms of the action of VB12 on the rhythm disorders are unknown. In the present study, therefore, effects of VB12 on circadian rhythms of locomotor activity were examined in mice. In the first experiment, CBA/J mice were maintained under continuous light condition (LL) or blinded, and after free-running rhythms became stable, the mice were intraperitoneally injected with either VB12 or saline at a fixed time every day. In all the mice with $\tau > 24$ h, saline injections resulted in entrainment of circadian rhythms, whereas not all the mice with $\tau < 24$ h entrained to the injection. In contrast to saline injections, VB12 injections did not always induce entrainment and about half of the mice with $\tau > 24$ h free-ran during the injection. In the second experiment, the amount of phase advances of circadian rhythms induced by a single injection of saline at circadian time (CT) 11 under LL was compared between the mice with and without VB12 silastic tubes. The results showed that the amplitude of phase advances was smaller in the mice with VB12 than those without VB12. In the third experiment, daily injections of saline were given to the mice with VB12 silastic tubes maintained under LL. In this chronic treatment of VB12 as well, attenuating effects of VB12 on saline-induced entrainment were observed. These results suggest that VB12 affects the mechanisms implicated in non-photic entrainment of circadian rhythms in mice.

Physiol Behav 1995 Jun;57(6):1019-24

Effects of intravenously administered vitamin B12 on sleep in the rat.

Chang HY, Sei H, Morita Y

Vitamin B12 (VB12) has been reported to normalize the entrainment of circadian rhythms in the non-24-h sleep wake cycle and delayed sleep phase insomnia in humans. The purpose of this work was to clarify whether the peripheral administration of VB12 has any sleep-promoting effect on the sleep-wake rhythm in freely moving rats. After a baseline day of saline infusion, VB12 (500 micrograms/kg/day) was administered continuously for 4 days via the jugular vein. Polysomnographic recordings were carried out concurrently. In both the light and the 24-h periods, the amount of non-rapid eye movement (NREM) sleep increased significantly on VB12-days 2 and 3, while the amount of REM sleep increased significantly on VB12-day 2. In the light period, the increase in NREM sleep was due to increased duration of the episode, while the tendency to an increase in REM sleep was due to an increased number of episodes. Changes in the diurnal sleep-wake rhythm tended to appear in the earlier light period. The serum VB12 concentrations in the VB12 group were 40 times higher than in controls. These findings suggest that peripherally infused VB12 has promoting effects on the rat's sleep, especially in the light period.

The following is novel and interesting. I would advise against supplementing with too much B12 because there is the possibility that too much B12 could deplete iron if iron is not concurrently supplemented.

DMSO and Vitamin B12

by Dr. David Gregg

There have been a number of publications reporting studies showing that breathing nitrous oxide may destroy a person's vitamin B12. This has been reported not only in journal articles, but has finally been incorporated in the latest books on nutritional supplements as well as books on biochemistry.

What first came to my mind was the use of this gas by dentists. Nitrous oxide, often called "laughing gas," is commonly used by dentists to help mitigate pain. This could present a risk to patients, but probably more often it presents a risk to people working in the office who would be exposed every day.

However, a far greater potential concern came to mind when I recently read a news article that stated that the catalytic converters in automobiles are creating enough nitrous oxide emissions to contribute significantly to the greenhouse effect. It is also known to be a very stable molecule that has a lifetime in the atmosphere of approximately 150 years.

With cars continuing to produce it, one would expect the concentration in the atmosphere, world wide, to be increasing every year, and it appears to be doing so. Is this already producing B12 deficiencies world wide, which will increase with time? This would not be surprising because we require (and absorb) only a few micrograms of vitamin B12 per day and our livers store only a few micrograms in reserve. It would take only a very low concentration of nitrous oxide in the atmosphere to destroy this if the destruction process is efficient, and the individual's dietary absorption process is inefficient. What are the potential health consequences and what can we as individuals do to protect against this potential problem? I have had some personal experience, which I will discuss below that makes me believe I have discovered a significant fraction of the population is B12 deficient. It is a far greater fraction that I would have expected, since it even exists in young people who should have healthy B12 absorption systems. Is this the effect of the atmospheric nitrous oxide emissions already showing up? I believe it is a definite possibility which deserves some serious attention.

Health Consequences of a Vitamin B12 Deficiency

It is widely recognized that vitamin B12 in combination with folic acid is essential for your body to synthesize hemoglobin. A deficiency can result in a particular form of anemia called pernicious anemia. However, as we continually expand our knowledge of biochemistry, it is being recognized that these vitamins fill far more broad ranging requirements. It is doubtful that all their functions been identified, but it is reasonable to conclude that a deficiency could result in or contribute to a broad range of degenerative processes.

The absorption of vitamin B12 requires a highly specialized process, which tends to become less effective with age. For this reason it is common for doctors to give elderly people B12 shots which result in them feeling much better and more energetic. It is also common for the elderly to develop numerous degenerative diseases. (They don't all get shots.) Does a B12 (and folic acid) deficiency contribute to the development of many degenerative diseases that we commonly associate with aging? It would not surprise me at all if it does. It doesn't appear to be so common to give vitamin B12 shots to young people, so we may have not discovered a deficiency that may exist. Is there a similar deficiency in younger people resulting in a different set of medical problems? I have reason to believe there might be, and my only explanation for such a surprising and unnatural development is the growing nitrous oxide concentration in the atmosphere.

The individual solutions and my evidence that the problem might be broad ranging over all age groups.

If a serious vitamin B12 deficiency is being caused by automobile emissions, we certainly want to change that process. However, this will require changes in cars that are beyond our individual control. So, what can we do individually?

I am a strong believer in oral dietary supplements. It is the best start. You can get B12 and folic acid supplements at any health food store and follow the directions on the label. Since vitamin B12 requires a special absorption system that may not be healthy in a particular individual, some people may not benefit from oral supplements. For such people, one form of B12 is available, called sublingual tablets, which are designed to be held under the tongue while the B12 is absorbed through the skin. Many may find this approach to be advantageous. Available by prescription are B12 shots, which may have to be administered by a doctor.

I discovered another approach which I experimented with personally and which eventually led me to discover what I interpreted to be a very common Vitamin B12 deficiency, independent of the age group. This surprised and puzzled me very much.

Back in 1994 when I was focusing on learning as much as I could about vitamin B12, an experiment came to mind, which I decided to try on myself. I saw a bottle of DMSO (dimethylsulfoxide) on the shelf of my health food store and remembered that DMSO is not only absorbed directly through the skin, but it also would carry with it any impurities dissolved in it. This can be a serious problem if the impurities are toxic. However, I also realized that if I dissolved vitamin B12 in it, it might carry it directly to my blood stream through my skin. I tried it and the results were dramatic for me, far greater than any impact I had ever felt from oral or sublingual tablets. I put some of my vitamin B12 tablets obtained at a health food store into a two liquid ounce bottle with an eyedropper and filled it with DMSO. It took a couple of days for the tablets to fall apart. Once they did, I put an eyedropper load on one arm and rubbed it in. In approximately one hour I started to feel very good, which was a sense of general strength and well being. This lasted all day. When I tried it again the next day, I got no such feeling. I also didn't experience any bad effects either. Since I knew that approximately one month's requirement of B12 is stored in the liver, I reasoned that my system was simply fully supplied with Vitamin B12 and that I wouldn't need to use it again for a month or so. When I tried it again a month or so later, I got a significant boost from it again. Since then I have continued to use it on a once every month or so basis.

With time I decided to also add folic acid and a multivitamin-multimineral tablet to give the solution a broader base of nutritional support. I use a two ounce bottle with an eyedropper, add 10mg of vitamin B12 (ten 1000 mcg tablets), 9.6 mg of folic acid (twelve 800 mcg tablets) and a single multivitamin-multimineral tablet and fill it with 99.9% DMSO (leaving a bubble at the top so it can be mixed when shaken). All ingredients were obtained from my local health food store. The tablets are mostly binder and take a few days to fall apart. They don't fully dissolve, but that doesn't seem to matter in terms of potency.

I now use this regularly on approximately a once every month or two basis. It serves as a reasonable mood elevator for me, and I believe it contributes significantly to my general health. My interpretation is I seem to become deficient in vitamin B12 even though I take oral supplements regularly.

Over time I have told a number of other people about this home method and many have chosen to try it. (I strongly recommended that they consult their physician first.) Of those who have chosen to make up solutions and try it, approximately 50% have told me that they noticed a very significant energy boost, and this was not limited to elderly people. It seemed to be independent of age, from age 25 and up.

Some also found a benefit if they used it as frequently as once every two weeks and others were like me, finding the best time span between use to be in the once-a-month or so range. If I interpret this to indicate B12 deficiencies, the 50% number is much higher than I would have expected, and the impact on young people was particularly unexpected. Is this an indication that there is something happening in our environment that is causing a broad base of Vitamin B12 deficiencies? When I read the news article about automobile exhaust and the production of enough nitrous oxide to affect the greenhouse effect, a light turned on. This may be the cause. If so, it is a very important issue.

It is my hope that this article will stimulate a thorough investigation into this issue to systematically evaluate if it is true, and result in an organized effort towards a solution.

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VITAMIN D AND SUNSHINE

I found that both vitamin D and sunshine helped me during my recovery. I particularly felt better after spending time in the sun, even though I was taking 6-8 capsules of vitamin A and D (10,000 IU of A, 400 IU of D per capsule). I shouldn't have been vitamin D deficient and if anything may have been taking too much A and D. However the added sunshine was always a plus. One member of our group who had a very persistent case of hyperT also reported that on vacations to sunny places where she was able to get into the sun every day she felt much better even though she stopped taking supplements for that week. JJ

"It was confirmed that TH (thyroid hormone) produced a peroxide of dehydrocholesterol, a precursor of vitamin D3, in the diaphysis of the femur in the increased metabolic state." [cadmium inhibits lipogenesis.doc](#)
Does this mean that thyroid hormone causes an increased peroxidation of pre-vitamin D and this is the mechanism by which hyperT causes calcium metabolism problems? JJ

Wilson's disease results in excess tissue accumulation of copper and is often complicated by skeletal and mineral abnormalities. We investigated *vitamin D* metabolism in rats fed a copper-laden diet rendering hepatic copper content comparable with that found in Wilson's disease. Injection of 25-hydroxyvitamin D3 [25(OH)D3] resulted in reduced 1,25-dihydroxyvitamin D [1,25(OH)2D] levels in copper-intoxicated rats. In vitro 25(OH)D-1 alpha-hydroxylase activity was impaired in renal mitochondria from copper-intoxicated animals. Activity was also inhibited in mitochondria from controls when copper was added to incubation media. Impaired conversion of 25(OH)D to 1,25(OH)2D occurs in copper intoxication and suggests that altered *vitamin D* metabolism is a potential factor in the development of bone and mineral abnormalities in Wilson's disease. [vitamin D metabolism impaired in Wilson.doc](#)

The following information indicates that vitamin D deficiency is involved in thyroid disease. Also, there are links to obesity, diabetes, cancer, heart disease, arthritis, depression, PMS, and autoimmune disease. The article is from Dr. Mercola's site at [mercola.com](#):

Breakthrough Updates You Need to Know on Vitamin D

The compound we call vitamin D can no longer properly be considered a vitamin. For most mammals, it is not in any sense even a nutrient. Nevertheless, vitamin D resembles true vitamins inasmuch as humans -- who are cut off from the critical solar ultraviolet wavelengths by reason of latitude, clothing, or shelter -- depend on an external source of the substance, just as they do for the true essential nutrients.

What is Vitamin D?

Vitamin D, calciferol, is a fat-soluble vitamin. It is found in food, but also can be made in your body after exposure to ultraviolet rays from the sun. Vitamin D exists in several forms, each with a different activity. Some forms are relatively inactive in the body, and have limited ability to function as a vitamin. The liver and kidney help convert vitamin D to its active hormone form.

The major biologic function of vitamin D is to maintain normal blood levels of calcium and phosphorus. Vitamin D aids in the absorption of calcium, helping to form and maintain strong bones. It promotes bone mineralization in concert with a number of other vitamins, minerals, and hormones.

Without vitamin D, bones can become thin, brittle, soft, or misshapen. Vitamin D prevents rickets in children and osteomalacia in adults, which are skeletal diseases that result in defects that weaken bones.

What are the sources of vitamin D?

Food sources

Fortified foods are the major dietary sources of vitamin D. Prior to the fortification of milk products in the 1930s, rickets (a bone disease seen in children) was a major public health problem in the United States. Milk in the United States is fortified with **10 micrograms (400 IU) of vitamin D per quart**, and rickets is now uncommon in the US.

Exposure to sunlight

Exposure to sunlight is an important source of vitamin D. Ultraviolet (UV) rays from sunlight trigger vitamin D synthesis in the skin.

Season, latitude, time of day, cloud cover, smog, and sunscreens affect UV ray exposure. For example, in

Boston the average amount of sunlight is insufficient to produce significant vitamin D synthesis in the skin from November through February.

Sunscreens with a sun protection factor of 8 or greater will block UV rays that produce vitamin D.

Vitamin D supplements are often recommended for exclusively breast-fed infants because human milk may not contain adequate vitamin D.

Vitamin D and Bone Health

It is estimated that over 25 million adults in the United States have, or are at risk of developing osteoporosis. Osteoporosis is a disease characterized by fragile bones. It results in increased risk of bone fractures.

Rickets and osteomalacia were recognized as being caused by vitamin D deficiency 75 years ago; their prevention and cure with fish liver oil constituted one of the early triumphs of nutritional science. The requirement for vitamin D has been pegged to these disorders ever since.

Having normal storage levels of vitamin D in your body helps keep your bones strong and may help prevent osteoporosis in elderly, non-ambulatory individuals, in post-menopausal women, and in individuals on chronic steroid therapy.

Researchers know that normal bone is constantly being remodeled (broken down and rebuilt). During menopause, the balance between these two systems is upset, resulting in more bone being broken down (resorbed) than rebuilt.

Vitamin D deficiency has been associated with greater incidence of hip fractures. A greater vitamin D intake from diet and supplements has been associated with less bone loss in older women. Since bone loss increases the risk of fractures, vitamin D supplementation may help prevent fractures resulting from osteoporosis.

The use of vitamin D is well accepted, but the mere absence of clinical rickets can hardly be considered an adequate definition either of health or of vitamin D sufficiency.

The fact that it takes 30 or more years to manifest itself makes it no less a deficiency condition than a disorder that develops in 30 days. It is easy to understand how long-period deficiency diseases could never have been recognized in the early days of nutritional science, but with modern methods and a better grasp of the relevant physiology, failing to recognize a slowly developing condition as a true deficiency state, can no longer be justified.

Vitamin D nutrition probably affects major aspects of human health, as listed below, other than its classical role in mineral metabolism. The rest of the article addresses some of the newly recognized uses of vitamin D.

Cancer

Today, it is well established that besides playing a crucial role in the establishment and maintenance of the calcium in the body, the active form of vitamin D also acts an effective regulator of cell growth and differentiation in a number of different cell types, including cancer cells.

Laboratory, animal, and epidemiologic evidence suggest that vitamin D may be protective against some cancers. Clinical studies now show vitamin D deficiency to be associated with four of the most common cancers:

- [Breast](#) (23)
- Prostate 24-27
- Colon 28-31
- Skin 32,33

Diabetes

Vitamin D deficiency has been associated with insulin deficiency and insulin resistance. (1-3) In fact, last year it was shown that vitamin D deficiency is likely to be a major factor for the development of type one diabetes in children. (4)

Heart Disease

Insulin resistance is also one of the major factors not only leading to the cancers mentioned above, but also to the number one killer in the US, heart disease. Northern countries have higher levels of heart disease and more heart attacks occur in the winter months. (5,6)

Arthritis

Progression of degenerative arthritis of the knee and hip is faster in people with lower vitamin D

concentrations (33-34)

Infertility and PMS

Infertility is associated with low vitamin D(7), and PMS has been completely reversed by addition of calcium, magnesium and vitamin D.(8)

Fatigue, Depression and Seasonal Affective Disorder

Activated vitamin D in the adrenal gland regulates tyrosine hydroxylase, the rate limiting enzyme necessary for the production of dopamine, epinephrine and norepinephrine.

Low vitamin D may contribute to chronic fatigue and depression. (9-10) Seasonal Affective Disorder has been treated successfully with vitamin D. In a recent study covering 30 days of treatment comparing Vitamin D and 2 hour daily use of 'light boxes', depression completely resolved in the D group, but not in the light box group.(11)

Autoimmune Disorders

Multiple Sclerosis, (12) Sjogren's Syndrome, rheumatoid arthritis, thyroiditis and Crohn's disease have all been linked with low vitamin D levels.

Single, infrequent, intense, skin exposure to UV-B light suppresses the immune system and causes harm.

However chronic low-level exposure normalizes immune function and enhances immune cell production. This reduces abnormal inflammatory responses such as found in autoimmune disorders, and reducing occurrences of infectious disease. (14-18)

Obesity

Vitamin D deficiency has been linked with obesity. (18, 19) Vitamin D has recently been shown to lower leptin secretion. (20) Leptin is a hormone produced by fat cells and is involved in weight regulation. It is thought that the hormone signals the brain when fat cells are "full," but exactly how the hormone controls weight is not entirely clear.

Additionally, obesity by itself probably further worsens vitamin D deficiency due to the decreased bioavailability of vitamin D(3) from skin and dietary sources, because of its being deposited in body fat. (36)

Syndrome X

Vitamin D deficiency has been clearly linked with Syndrome X. (21) Syndrome X refers specifically to a group of health problems that can include insulin resistance (the inability to properly deal with dietary carbohydrates and sugars), abnormal blood fats (such as elevated cholesterol and triglycerides), overweight, and high blood pressure.

Vitamin D and Steroids

Steroids, like prednisone, are often prescribed to reduce inflammation from a variety of medical problems. These medicines may be essential for a person's medical treatment, but they have potential side effects, including decreased calcium absorption.

There is some evidence that steroids may also impair vitamin D metabolism, further contributing to the loss of bone and development of osteoporosis associated with steroid medications. For these reasons, individuals on chronic steroid therapy should consult with their physician or registered dietitian about the need to increase vitamin D intake through diet and/or dietary supplements.

The above document was edited from:

[National Institutes of Health Document on Vitamin D](#)

DR. MERCOLA'S COMMENT:

I wish to express my sincere appreciation to nutritionist Krispin Sullivan for the years she researched this subject, which provided me with so much of the foundational background for this review. She is publishing the definitive resource for vitamin D later this year called [Naked at Noon](#).

A preliminary copy of her vitamin D research is available on her [web site](#).

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VITAMIN E

Thyroidal function: Vitamin E facilitates selenium metabolism and is therefore critical for normal thyroid function. Excessive supplementation of vitamin E without selenium may deplete selenium and therefore contribute to thyroid disease (both hypo and hyper).

Rough file:

Long-Evans Cinnamon (LEC) rats are autosomal recessive mutants that develop hepatitis and hepatocellular carcinoma. Because copper accumulates in the livers of these rats, and some of their clinical and pathological features are similar to those of patients with Wilson's disease, LEC rats are proposed as an animal model of Wilson's disease. To examine the effects of **vitamin E** as an antioxidant on hereditary hepatitis in LEC rats, we fed 3-week-old rats for 25 weeks either **vitamin E**-deficient, control, or **vitamin E**-supplemented diets which contained < 0.01 mg of total tocopherols, 2 mg of d,l-alpha-tocopheryl acetate (2 I.U.), and 58.5 mg of d,l-alpha-tocopheryl nicotinate (50 I.U.), respectively, per 100 mg of feed. In males, body weight loss was first observed in the **vitamin E**-deficient group, and mean ages at which jaundice occurred were in the order: deficient younger than control younger than supplemented groups. The ages when plasma glutamic oxaloacetic transaminase and glutamic pyruvic transaminase activities began to increase sharply and peaked followed the same order. Thus, it is likely that free radicals are involved in jaundice and hepatitis in LEC male rats, and they are a model for studying the relationship of copper, free radicals, and hepatitis. Conversely, in females, no apparent differences in clinical and biochemical changes were observed among the three groups. Causes for the discrepancy between the sexes remain to be clarified. [vitamin E decreases hepatitis in LEC male rats, not females.doc](#)

The ratio of serum **vitamin E** to serum lipids (cholesterol, triglycerides, phospholipids) was highest in healthy controls and in patients in group A with cirrhosis and normal transaminases and bilirubin. Patients in group A with acute or chronic ethanol intoxication and high bilirubin levels had a 37% lower lipid-standardized **vitamin E** level than controls. Patients in group B with hemochromatosis, showing high serum iron (> 180 micrograms/dl), a low free iron binding capacity (< 8 mumol/l) and high ferritin-levels (< 450 micrograms/l), had a 34% lower **vitamin E**/lipid ratio than healthy controls. No significant lowering of the **vitamin E**/lipid ratio was observed in the other patients in group B. A significant decrease (37%) in the **vitamin E**/lipid ratio was only detectable in patients with Wilson's disease (group C) showing high free serum copper (> 10 micrograms/dl). The data support a role for free radicals in the pathogenesis of active liver diseases. [vitamin E low in cirrhosis, hemochromatosis, & Wilson's.doc](#)

OBJECTIVE: Oxygen free radicals (OFR) play a role in the pathogenesis of tissue damage in many pathological conditions via the peroxidation of membrane phospholipids. Experimental studies showed an elevated oxidative stress during hyperthyroidism, which is reduced by treatment. Therapy per se might decrease oxidative stress. DESIGN: Fasting plasma levels of thiobarbituric acid reacting substances (TBARS), vitamin E and coenzyme Q10 were measured in 22 hyperthyroid patients, before treatment for their thyroid disease, after 13.9 [SD 9.2] weeks, when they achieved an euthyroid state on thyrostatic drugs, and again after 47.7 [21.0] weeks, off therapy. No patient presented additional risk factors for increased lipoperoxidation and/or increased OFR levels. Smokers were asked to abstain from smoking overnight. METHODS: All analytes were measured by HPLC. RESULTS: In hyperthyroidism, plasma levels of TBARS were increased, whereas vitamin E and coenzyme Q10 were reduced. Average levels of TBARS and antioxidant agents returned to normal in euthyroid patients, without differences in relation to stop of thyrostatic therapy. CONCLUSIONS: Our data confirm the presence of oxidative stress and decreased antioxidant metabolites in hyperthyroid patients, which are corrected in euthyroidism, without any influence of thyrostatic drugs per se. Nutritional support with antioxidant agents, which are defective during hyperthyroidism, is warranted. [vitamin E and Co-Q-10 deficient in hyperT.doc](#)

Some Vitamin E Supplements May Increase Prostate Cancer Risk

Men with high blood levels of gamma-tocopherol, a form of vitamin E not usually found in vitamin supplements, have a reduced risk for prostate cancer. However, **many vitamin E supplements contain only alpha tocopherol, which can actually lower levels of gamma tocopherol.**

- Researchers looked at blood samples taken from nearly 10,500 men.
- The 20% with the highest levels of gamma-tocopherol were **five times less likely** than men with the lowest levels of the vitamin to get prostate cancer over the next seven years.

Vitamin E is found naturally in vegetable and seed oils, nuts, whole grains and leafy greens, but levels of the different forms of vitamin E vary.

Men with high levels of alpha-tocopherol and the mineral selenium, were less likely to develop prostate cancer only when gamma-tocopherol was also high, suggesting gamma-tocopherol boosts the power of the other two antioxidants.

In an editorial accompanying the report, Dr. Edward Giovannucci of Harvard Medical School in Boston, Massachusetts calls the findings "further reason for optimism" that vitamin E and other compounds may fight prostate cancer.

However, he notes that some vitamin E supplements--mainly alpha-tocopherol--can lower blood levels of gamma-tocopherol. According to Dr. Giovannucci, the average American's bloodstream is five times richer in alpha-tocopherol than gamma-tocopherol. And, **that difference jumps to 20-fold among people who take vitamin E supplements**

Since vitamin E supplements may displace gamma-tocopherol, the researchers conclude,

future studies aimed at prostate cancer prevention should include both forms of vitamin E.

Journal of the National Cancer Institute, December 20, 2000; 92: 44-49

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DRINKING WATER

It seems to me that most people who have thyroid disease, especially hyperthyroidism, are drinking bottled water. This is something that concerns me. I don't have any scientific studies to support my beliefs but I feel that the water we drink is very important and this topic needs to be discussed.

When I developed hyperthyroidism I was drinking distilled water. I had been drinking this for many years and thought that this should be benefiting my health because it is the purest water available. Now, however, I feel that drinking distilled water is probably one of the worst things that you can do to your health.

Once I reasoned that thyroid disease is primarily caused by mineral deficiencies, I switched from drinking distilled water to drinking bottled "drinking water", i.e. purified water with minerals still retained. I felt that this was a significant part of my recovery.

Distilled water enters the body with no minerals but leaves the body with minerals. The net result is that your body continuously loses minerals and must make up this loss with the minerals in foods and drinks. Since I was a purest, like many people, I didn't drink sodas, coffee, or tap water served in restaurants which is usually made from tap water. Most people who drink bottled water at home probably consume other (mineralized) water and this helps their mineral status. My purest beliefs probably contributed more to my loss of essential minerals.

When I was really sick I questioned the purity of the distilled water that I was drinking and bought a home water distiller. After a week of drinking this water I was so much sicker I stopped using the distiller. Because the distiller has an aluminum electrode and aluminum might be light enough to pass through the condensing pipe it's possible the water contained aluminum and this was the reason for my deterioration, but more than likely it was the lack of all minerals in this water.

I feel that drinking tap water, even with the chlorine and other purification chemicals added, is probably better for health than drinking either distilled water or bottled water which is deficient in the heavier minerals.

You may want to check the source of the water in the municipal supply where you live (and there may be valid reasons for not drinking that water), but in the Los Angeles area the water comes from the Sierra Nevada mountains. This water percolates down through the mineral rich rock of the mountains and probably contains many valuable minerals.

I used to take 10 5-gallon bottles with me to Mammoth every year and fill them up with water from our friends' artisan well. I was convinced that this water kept me healthy and I was able to drink this water about 6 months out of the year. At the time we drove a Suburban (with the three kids) and had room for all these bottles. However, when the two older kids went off to college we no longer needed a large vehicle so I abandoned the practice in 1996. In 1997 I developed hyperthyroidism after the first winter without this mountain water.

Our friends in Mammoth own the local health food store and are very knowledgeable about nutrition. Lately my research has led me to the hypothesis that the mineral tungsten is critical for copper metabolism (many reasons and long story) and that a tungsten deficiency may be involved in hyperthyroidism. When I told my friend Nick about this he was very interested and told me that all the mountains in that area above his well are very high in tungsten and there is a tungsten mine in that area. This of course really intrigued me.

Because of their position in the community owning the health food store, my friends are very familiar with the health problems in that area. They knew of only one person with hyperthyroidism there and only two people with psychiatric problems. I asked about the latter because schizophrenia also seems to be a disease caused by a breakdown of copper metabolism and is probably the result of a deficiency of some trace element involved in copper metabolism. In schizophrenics, copper builds up in the body and liver, and is not being used properly. A high percentage of schizophrenics have hyperthyroidism.

While I'm not sure about the person with hyperthyroidism, my friends told me that the two people with schizophrenia drank bottled water and not the local water (the local water has chlorine so some people don't drink it.)

While I may be off on a wild goose chase, I now have many reasons to suspect that tungsten, which is probably in the water coming from any granite mountains, may be a critical nutrient for copper metabolism and therefore needed by people with thyroid disease (both hypers and hypos).

Tungsten, unfortunately, is not a mineral which is sold as a supplement in health food stores. I am going to get my compounding pharmacist to obtain some for me for testing after I determine the best compound.

The best other sources of tungsten are probably drinking water that comes from mountains, even if this means drinking chlorinated tap water, or a good trace element supplement. You can remove much of the chlorine by either filtering or leaving the water out in a glass bowl for a week or so.

For trace elements, I always found that the one sold by New Vision (order through www.newvision.com) worked the best for me. When I became interested in tungsten, I looked at an analysis of New Visions' trace mineral supplement and it seems to contain a fair amount. (I hope to add more information soon about trace mineral supplements under Nutrients and Toxics/Minerals/Trace Minerals on this site.)

As I learn more about the mineral content of different drinking waters I will add that information here. If the water from my friends' well proves to have benefits for those with thyroid disease (I intend to get it analyzed for mineral content), then that may be the water to drink. If we find this is true and the key ingredient is tungsten then we may be able to solve the problem by just taking a tungsten supplement (I'll be working on that also).

This is an interesting story and I'll keep you informed. John

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ZINC

Zinc and Thyroid function.

Zinc increases thyroid function and is usually high in hypers and low in hypos. Studies show that hypers usually have low zinc in the blood and this information seems to be the source of the very common nutritional advice that hypers need zinc. I have found that this is exactly the wrong thing to do in most cases. Some hypers are deficient in both copper and zinc, but usually even these persons should start supplementing with copper first, before zinc supplementation is begun. Generally for hyperthyroidism, copper should be supplemented first, then iron, and then zinc only if necessary. For hypothyroidism, zinc should be supplemented first (along with selenium). When nighttime rapid heart beat begins, then iron and copper should be added.

One unsuspected zinc source:

Some sunscreens use zinc as a physical sun block and I have these to avoid the dangerous chemicals present in most sun screens. However, I noticed that often I would get an increase in hyper symptoms after being in the sun. I now think that the zinc from the sun screen is absorbed into the body and can be a significant source of zinc, and therefore a possible cause of hyperthyroidism.

J Nutr 2000 May;130(5S Suppl):1378S-83S

Dietary factors influencing zinc absorption.

Lonnerdal B

Department of Nutrition, University of California at Davis, Davis, CA 95616-8669, USA.

Marginal zinc deficiency and suboptimal zinc status have been recognized in many groups of the population in both less developed and industrialized countries. Although the cause in some cases may be inadequate dietary intake of zinc, inhibitors of zinc absorption are most likely the most common causative factor. Phytate, which is present in staple foods like cereals, corn and rice, has a strong negative effect on zinc absorption from composite meals. Inositol hexaphosphates and pentaphosphates are the phytate forms that exert these negative effects, whereas the lower phosphates have no or little effect on zinc absorption. The removal or reduction of phytate by enzyme (phytase) treatment, precipitation methods, germination, fermentation or plant breeding/genetic engineering markedly improves zinc absorption. Iron can have a negative effect on zinc absorption, if given together in a supplement, whereas no effect is observed when the same amounts are present in a meal as fortificants. Cadmium, which is increasing in the environment, also inhibits zinc absorption. The amount of protein in a meal has a positive effect on zinc absorption, but individual proteins may act differently; e.g., casein has a modest inhibitory effect of zinc absorption compared with other protein sources. Amino acids, such as histidine and methionine, and other low-molecular-weight ions, such as EDTA and organic acids (e.g., citrate), are known to have a positive effect on zinc absorption and have been used for zinc supplements. Knowledge about dietary factors that inhibit zinc absorption and about ways to overcome or remove these factors is essential when designing strategies to improve the zinc nutrition of vulnerable groups.

Title

Zinc, the brain and behavior.

Author

Pfeiffer CC; Braverman ER

Source

Biol Psychiatry, 17(4):513-32 1982 Apr

Abstract

The total content of zinc in the adult human body averages almost 2 g. This is approximately half the total iron content and 10 to 15 times the total body copper. In the brain, zinc is with iron, the most concentrated metal. The highest levels of zinc are found in the hippocampus in synaptic vesicles, boutons, and mossy fibers. Zinc is also found in large concentrations in the choroid layer of the retina which is an extension of the brain. Zinc plays an important role in axonal and synaptic transmission and is necessary for nucleic acid metabolism and brain tubulin growth and phosphorylation. Lack of zinc has been implicated in impaired DNA, RNA, and protein synthesis during brain development. For these reasons, deficiency of zinc during pregnancy and lactation has been shown to be related to many congenital abnormalities of the nervous system in offspring. Furthermore, in children insufficient levels of zinc have been associated with lowered learning ability, apathy, lethargy, and mental retardation. Hyperactive children may be deficient in zinc and *vitamin* B-6 and have an excess of lead and copper. Alcoholism, schizophrenia, Wilson's disease, and Pick's disease are brain disorders dynamically related to zinc levels. Zinc has been employed with success to treat Wilson's disease, acrodermatitis enteropathica, and specific types of schizophrenia.

Zinc excretion is high in hyperthyroidism, suggesting that the body is trying to get rid of excess zinc. In hypothyroidism, zinc excretion is low.

Title

[Alterations of *zinc* levels in patients with thyroid disorders]

Author

Tsou CT; Chen MD; Lin WH; Ho LT

Address

Department of Medicine, Taichung Veterans General Hospital.

Source

Chung Hua I Hsueh Tsa Chih (Taipei), 51(1):57-60 1993 Jan

Abstract

It is known that patients with hyperthyroidism have a lower *zinc* content in their erythrocytes, and that this decrement returns to normal after treatment with anti-thyroid drugs. This study was designed to investigate the alteration of body *zinc* levels in thyroid disorder. Two groups of out-patients associated with hyperthyroidism or hypothyroidism, and a group of normal healthy controls were collected. *Zinc* contents in the blood, hair and 24-hour urine samples were determined by a flame atomic absorption spectrometer. The results showed that patients with hyperthyroidism had a lower erythrocyte *zinc* level and an increased urinary *zinc* excretion ($p < 0.05$). The hypothyroidism had a higher hair *zinc* content and a decrement in urinary *zinc* excretion ($p < 0.05$). Body *zinc* levels, excluding the plasma *zinc*, held a certain correlation to the plasma thyroid hormones levels. The urinary *zinc* levels showed a more parallel variation in the thyroid disorders ($p < 0.05$). This data indicates that the alteration of urinary *zinc* levels might be a useful index for thyroid disorder evaluation. Body *zinc* could also play a physiological role in the metabolic regulation(s) of a thyroid disorder.

Title

Erythrocyte *zinc* in hyperthyroidism: reflection of integrated thyroid hormone levels over the previous few months.

Author

Yoshida K; Kiso Y; Watanabe TK; Kaise K; Kaise N; Itagaki Y; Yamamoto M; Sakurada T; Yoshinaga K

Address

Department of Clinical Biology and Hormonal Regulation, Tohoku University School of Medicine, Sendai, Japan.

Source

Metabolism, 39(2):182-6 1990 Feb

Abstract

Red blood cell (RBC) *zinc* (Zn) concentration was measured by atomic absorption spectrophotometry in 28 healthy volunteers, in 46 patients with hyperthyroidism, and in 6 patients with hypothyroidism. The mean (\pm SD) RBC Zn concentration in euthyroid controls was 11.4 \pm 1.5 mg/L RBC, and the normal range defined as the mean \pm 2 SD was 8.5 to 14.3 mg/L RBC. The mean RBC Zn in patients with hyperthyroidism was decreased to 6.4 \pm 1.6 mg/L RBC, and 43 (93%) had low values. The mean RBC Zn in patients with hypothyroidism was not different from that in the controls. There was a significant negative correlation between the concentrations of RBC Zn and those of both plasma thyroxine (T4; $r = -0.73$) and plasma 3,5,3'-triiodothyronine (T3; $r = -0.70$). After the treatment of 17 hyperthyroid patients with antithyroid drugs, both mean plasma T4 and T3 levels became normal within 4 weeks, but the normalization of RBC Zn lagged about 2 months behind them. The RBC Zn levels significantly correlated with both the plasma T4 and T3 levels obtained 0, 4, 8, and 12 weeks prior to the RBC sampling, and the highest correlation was observed between the RBC Zn levels and plasma T4 and T3 levels measured 8 weeks previously. These data suggest that RBC Zn concentration in hyperthyroid patients reflects a patient's mean thyroid hormone level over the preceding several months as glycosylated hemoglobin level does in diabetic patients.

Zinc increases the immune response.

Zinc deficiency causes an increase in brain norepinephrine.

Title

Influence of dietary *zinc* on rat brain catecholamines.

Author

Wallwork JC; Botnen JH; Sandstead HH

Source

J Nutr, 112(3):514-9 1982 Mar

Abstract

Weanling rats were fed a 20% sprayed egg white, *zinc*-deficient diet for 9 or 10 days. One group (*zinc*-deficient) was fed ad libitum and given distilled deionized water; a second group was individually pair-fed to rats in the *zinc*-deficient group; a third group was fed ad libitum; a fourth group was also fed ad libitum, but was fasted overnight prior to slaughter. The latter three groups were given 25 ppm *zinc* (as *zinc* acetate) in the water. The brain was excised and the catecholamines were extracted with 0.1 M perchloric acid separated by reverse phase HPLC and measured electrochemically. There did not appear to be a correlation between food intake and brain catecholamine concentrations in any of the groups examined. **Brain norepinephrine concentrations in the zinc-deficient rats, however, were significantly higher than in the pair-fed or ad libitum-fed rats.**

The following study shows that zinc absorption increased by B-6 and picolinic acid and decreased by dietary iron.

Title

Effect of iron, vitamin B-6 and picolinic acid on *zinc* absorption in the rat.

Author

Evans GW; Johnson EC

Source

J Nutr, 111(1):68-75 1981 Jan

Abstract

True daily *zinc* absorption was determined in rats fed a high iron diet (220 ppm Fe; 16.5 ppm Zn), and adequate iron diet (30 ppm Fe) and a high iron diet with varying levels of pyridoxine-HCl (2-40 ppm). **Zinc absorption in rats fed the high iron diet was significantly less than in rats fed the adequate iron diet.** *Zinc* absorption in rats fed the high iron diet supplemented with picolinic acid (200 ppm) was markedly increased and did not differ from that in rats fed the adequate iron diet. **True, daily zinc absorption increased as the level of dietary vitamin B-6 was increased. Zinc absorption was the least in rats fed 2 ppm vitamin B-6 and was greatest in rats fed 40 ppm vitamin B-6.** The concentration of picolinic acid in the pancreas increased as the level of dietary vitamin B-6 was increased. *Zinc* absorption was significantly elevated in rats fed the high iron diet that contained either 4 or 10 ppm vitamin B-6 and 200 ppm picolinic acid. The turnover rate of ⁶⁵Zn was determined in rats fed an adequate iron, marginal *zinc* diet (8.5 ppm Zn) with varying levels of vitamin B-6. The turnover of ⁶⁵Zn was greatest in rats fed 2 ppm vitamin B-6 and least in rats fed 40 ppm vitamin B-6 or 2 ppm vitamin B-6 + 200 ppm picolinic acid. **The results suggest that high levels of dietary iron inhibit zinc absorption via competition for binding with endogenous picolinic acid. The results provide further evidence to support the hypothesis that picolinic acid facilitates absorption of dietary zinc.**

In the following study guinea pigs were made zinc deficient. The animals showed "depression with abnormal posture, scaly skin lesions on various parts of the body, oedematous swelling on hind limbs and marked alopecia." Also, the thyroid hormones, T4 and T3, decreased and the thyroid gland decreased in size.

Title

Effect of experimental *zinc* deficiency on thyroid gland in guinea-pigs.

Author

Gupta RP; Verma PC; Garg SL

Address

Department of Veterinary Pathology, Haryana Agricultural University, Hisar, India.

Source

Ann Nutr Metab, 41(6):376-81 1997

Abstract

Zinc deficiency was produced experimentally in guinea-pigs fed on a diet containing 1.03 mg Zn/kg over a period of 45 days. **Clinical signs exhibited in Zn-deficient (ZnD) animals were depression with abnormal posture, scaly skin lesions on various parts of the body, oedematous swelling on hind limbs and marked alopecia.** There was no effect on food intake. **Serum studies in ZnD group revealed significant decreases in the concentrations of Zn from 20 days onwards, and tri-iodo-thyronine (T3) and thyroxine (T4) from 30 days onwards.** Thyroid glands of ZnD animals were smaller in size and pale or whitish pale in colour. Histopathologically, these glands showed changes of atrophy and degeneration in the follicles. It could be concluded that the depletion in serum T3 and T4 due to Zn deficiency was related to thyroid lesions.

Title

Pathologic changes, tissue distribution, and extent of conversion to ethylenethiourea after subacute administration of *zinc* ethylene-bis-dithiocarbamate (zineb) to calves with immature rumen function.

Author

Nebbia C; Ferrero E; Valenza F; Castagnaro M; Re G; Gennaro Soffietti M

Address

Department of Animal Pathology, Faculty of Veterinary Medicine, University of Turin, Torino, Italy.

Source

Am J Vet Res, 52(10):1717-22 1991 Oct

Abstract

The toxicity of zinc ethylene-bis-dithiocarbamate (zineb), a widely used fungicide, was studied in four 4-week-old Friesian calves with immature rumen function. Calves were first subjected to liver biopsy, and thereafter, 3 of them were orally administered 200 mg of zineb/kg of body weight daily for 80 days, whereas the fourth calf served as control and remained untreated. Clinical, hematologic, and pathologic (including ultrastructural) findings were recorded. The distribution in body fluids and tissues of the parent compound and one of its main metabolites, ethylenethiourea (ETU), also was examined. **Treated calves had unthrifty appearance and reduction in weight gain. They also had remarkable impairment of thyroid function, as reflected by reduction in serum concentrations of triiodothyronine and thyroxine and increase in weight of the thyroid gland associated with epithelial vacuolization and foci of hyperplasia.** Moderate increase in liver glycogen content and impairment in maturation of germ cells were recorded consistently. Whereas zineb was widely distributed in body tissues, ETU accumulated mainly in the liver and the thyroid gland, although noticeable concentrations also were attained in muscle. Data were consistent with involvement of ETU mainly in the pathogenesis of thyroid gland lesions, and indicate that unweaned calves given zineb develop a clinicopathologic syndrome that does not differ qualitatively from that already described in adult cattle exposed to zineb.

In zinc deficient rats, the production of thyroid hormones decreases, but there is a compensatory increase in deiodination activity (the enzymatic conversion of T4 to T3). Interestingly (if my interpretation of this study is correct) the zinc deficient animals were more resistant to the effect of thiouracil, which is an antithyroid similar to PTU which reduces deiodinase activity.

This may relate to humans in this way: if a person with hyperthyroidism is deficient in zinc, then PTU (or Tapazole) may not work well to reduce the thyroid hormone level. Thus in instances when PTU or Tapazole are not reducing the thyroid hormone levels, zinc deficiency should be suspected.

This may explain my personal experience with PTU, which was that I would be relieved of hyper symptoms within 30-60 minutes. I was supplementing zinc and probably had very high body zinc levels. Other hyperts have reported that it has taken weeks to obtain benefit from PTU.

Title

Effects of *zinc* deficiency on thyroid function.

Author

Oliver JW; Sachan DS; Su P; Applehans FM

Source

Drug Nutr Interact, 5(2):113-24 1987

Abstract

Interactive combinations of altered *zinc* and thyroid states were studied in rats to assess pathophysiologic effects. Clinical signs of *zinc* deficiency or thyroid alteration were limited to effects on growth rate. Changes in organ and glandular weights and serum thyrotropin levels reflected changes in serum thyroid hormone concentrations. **Significantly (probability less than .001), zinc-deficient rats had enhanced hepatic thyroxine-5'-monodeiodinase activity. In addition, the zinc-deficient state was found to be protective against thiouracil-induced suppression of the microsomal-monoxygenase and thyroxine-5'-monodeiodinase enzyme complex. This protective effect was evident**

by greater thyroxine-5'-monodeiodinase and reduced nicotinamide-adenine dinucleotide phosphate cytochrome c reductase activities, as well as cytochrome P-450 content, in zinc-deficient/thiouracil-treated animals. Thus, the enzyme complex had increased triiodothyronine-generating capacity in conditions of *zinc* deficiency, which may be important because of the greater biological reactivity of triiodothyronine. Primary *zinc* deficiency conditions of the magnitude seen in this study and in this-age rat did not appear to alter serum thyroid hormone levels or organ/glandular function. However, concurrent *zinc* deficiency and altered thyroid status did change thyroid hormone response and disposition, which may be important to populations at risk because of thyroid dysfunctional states.

In the following study, high doses of the zinc compound Zineb caused an increase in thyroid activity in rats.

Title

Dose effect relationship for some specific effects of dithiocarbamates.

Author

Kaloyanova F; Ivanova-Chemishanska L

Address

Research Institute of Hygiene and Occupational Health-Sofia, Bulgaria.

Source

J Hyg Epidemiol Microbiol Immunol, 33(1):11-7 1989

Abstract

The effect of *zinc* ethylenebisdithiocarbamate (zineb) and manganese ethylenebisdithiocarbamate (maneb) has been studied in a chronic experiment (4.5 months) on albino rat thyroid gland and gonads. A complex of biochemical, morphological (histological, histochemical and electronmicroscopic), radiological, functional and biological methods has been employed. Different groups of rats were subjected to inhalatory poisoning with zineb in concentrations 110, 50, 10 and 2 mg.m-3 and maneb in concentrations 135, 12 and 2 mg.m-3. It was established that both compounds provoke toxic irritative changes in the lung and the trachea, more strongly expressed with maneb. A correlation of the dose and the effect was determined. **At a zineb dose 0.1 LD50 and 0.01 LD50 applied twice weekly an increased 131I uptake (rebound phenomenon) was found and signs of increased activity of the thyroid gland.** At doses 0.1, 0.02 and 0.01 LD50 both for zineb and maneb and an additional dose 0.002 LD50 for maneb, a decrease in the fertile capacity resulting from the damage of the germinative was determined (atrophic changes in Sertoli cells, deserted tubuli seminiferi because of disturbed maturation of the spermatozoa; small number or lack of differentiated forms of spermatogenesis; suppressed ovopoiesis, increased number of atretic follicles, with the domination of the relative part of the growing follicles) and endocrinoactive structures (destruction to disappearing of Leydig's cells; injured cells of Theca interna, granulosa and interstitium). These data as well as the data for teratogenicity give us grounds to recommend a higher security coefficient in hygiene standardization.

In the following study rats were made zinc deficient. Since zinc deficiency causes a decrease in food intake, control rats were fed the same amount of food to control for food intake. T4 and T3 levels in both groups declined, but T3 levels in the zinc deficient rats declined more than in the zinc adequate rats. Iodine uptake was similar between the two groups. This suggests that zinc deficiency interferes with the deiodinase enzyme conversion of T4 to T3.

Title

Zinc deficiency, chronic starvation, and hypothalamic-pituitary-thyroid function.

Author

Morley JE; Gordon J; Hershman JM

Source

Am J Clin Nutr, 33(8):1767-70 1980 Aug

Abstract

Male Sprague-Dawley rats were fed a *zinc*-deficient diet to study its effects on the hypothalamic-pituitary-thyroid axis. **As zinc-deficient animals fail to gain weight, they were compared to pair-fed growth restricted animals as well as ad libitum fed controls.** The growth velocity curves were superimposable for the *zinc*-deficient animals and the pair-fed controls; both were markedly reduced compared to the ad libitum controls. **Both the zinc-deficient and the pair-fed controls had lower triiodothyronine (T3) and thyroxine levels compared to the ad libitum controls. In addition T3 values were lower in the zinc-deficient animals compared to the pair-fed controls (P < 0.05).** Hypothalamic thyrotrophin-releasing hormone content was decreased in the *zinc*-deficient rats (162 +/- 32 pg/ml) compared to the ad libitum controls (305 +/- 102; P < 0.01). The 125I thyroidal uptakes were not significantly different between the *zinc*-deficient and the pair-fed controls. **Zinc deficiency lowers T3 more than comparable caloric restriction; this suggests that zinc deficiency may impair extrathyroidal production of T3.**

The following study shows that high zinc intake decreases copper content of various organs.

Title

Concentration of minerals in tissues of pigs from dams fed different levels of dietary *zinc*.

Author

Hill GM; Miller ER; Whetter PA; Ullrey DE

Source

J Anim Sci, 57(1):130-8 1983 Jul

Abstract

Effects on the tissue mineral concentrations of pigs from sows fed four dietary Zn levels were studied. A male and a female from first- and second-parity litters were killed at 1 and 21 d of age. The dams were fed a corn-soybean meal basal diet supplemented with 0, 50, 500 or 5,000 ppm Zn from 30 kg body weight until completion of the second lactation. **Pigs from sows fed 5,000 ppm additional zinc had heavier liver, heart, thyroid and adrenal weights relative to their body weight than did pigs from sows on the other treatments.** First- and second-parity pigs from sows on the highest Zn supplementation level had higher Fe stores in the liver, higher Zn concentrations in the liver, kidney and pancreas, and higher Cu levels in the kidney compared with pigs from sows on the other treatments. However, **Cu concentrations in the liver, heart, pancreas, esophagus, aorta and testes were reduced in pigs from sows on the 5,000 ppm Zn treatment.** In first-parity pigs, Ca in the liver was higher for pigs whose dams received 5,000 ppm Zn compared with pigs from sows on all other treatments, and the Mn level was higher compared with pigs from sows receiving 50 or 500 ppm additional *zinc*. Pigs at 1 d of age from sows on the 0, 50 or 500 ppm

treatment had lower hepatic P and Zn concentrations than pigs from sows on the same treatment at 21 d of age. The reverse was true for pigs whose dams received 5,000 ppm Zn.

The following study shows that an iodine deficiency reduces thyroid hormone levels and induces goiter. However a concurrent marginal zinc deficiency does not increase the effects from an iodine deficiency. This indicates that there are no significant zinc and iodine interactions.

Title

Thyroid function in rats with iodine deficiency is not further impaired by concurrent, marginal *zinc* deficiency.

Author

Smit JG; van der Heide D; van Tintelen G; Beynen AC

Address

Department of Human and Animal Physiology, Agricultural University, Wageningen, The Netherlands.

Source

Br J Nutr, 70(2):585-92 1993 Sep

Abstract

The hypothesis tested was that Zn deficiency aggravates impaired thyroid function as induced by I deficiency. In two separate experiments male rats were fed on diets either deficient in Zn or in I, or deficient in both. An identical, restricted amount of food was given to each rat so that body-weight gain of the experimental groups was comparable. **Zn deficiency was evidenced by reduced tibial Zn concentrations. I deficiency was evidenced by goitre, reduced urinary I excretion, reduced plasma thyroxine concentrations and reduced absolute amounts and concentrations of thyroxine in the thyroid. Zn deficiency had no effect on the raised thyroid weight as induced by I deficiency.** Zn restriction from 184 $\mu\text{mol Zn/kg}$ diet to 31 $\mu\text{mol Zn/kg}$ diet, but not to 92 $\mu\text{mol Zn/kg}$ diet, significantly lowered plasma thyroxine concentration. **There were no interrelated effects of Zn and I deficiencies on thyroid hormone levels. These results indicate that marginal Zn deficiency does not influence thyroid hormone metabolism in I deficiency.**

Following is an interesting study comparing the effects of zinc supplementation on thyroid hormone levels in genetically obese mice and normal lean mice. Obese mice normally have lower T4, T3, and deiodinase activity than lean mice. While zinc supplementation reduced blood levels of T4 in both groups, only the obese mice had lowered T4, T3, and deiodinase levels in the liver. Interestingly zinc decreased the liver deiodinase activity in all mice.

This study is in contradiction to my conception and the results of other studies which indicate that zinc increases the deiodinase activity. There may be other uncontrolled factors that affected these results, but it's important to look at all studies to try to understand what's going on.

Title

Zinc supplementation on serum levels and hepatic conversion of thyroid hormones in obese (ob/ob) mice.

Author

Chen MD; Lin PY; Lin WH

Address

Division of Endocrinology and Metabolism, Taichung Veterans General Hospital, Taiwan, ROC.

Source

Biol Trace Elem Res, 61(1):89-96 1998 Jan

Abstract

The supplemental effects of *zinc* on thyroid status in obese (ob/ob) mice were studied. Four-week-old obese mice and their lean controls were fed either a basal diet or a *zinc*-supplemented diet (200 mg/kg diet) for 8 wk. **Following the 8-wk basal diet, obese mice had lower serum T4 values, as well as hepatic T4 and T3 values, than lean mice ($p < 0.05$). A significant decrease in hepatic 5'-deiodinase activity was also observed in obese mice. Dietary zinc supplementation significantly reduced serum T4 levels in both the obese and lean mice. However, the zinc-supplemented effects on diminishing hepatic T4 and T3 values, as well as on 5'-deiodinase activities, were found only in obese mice ($p < 0.05$).** Furthermore, the 5'-deiodinase activities in hepatic microsomal pellets after incubation with various *zinc* concentrations (0.5, 1.0, and 2.5 mM) were also examined. **The 5'-deiodinase activities, in hepatic samples from all mice, were significantly attenuated by zinc treatments.** However, this effect was more predominant in obese mice following the addition of 0.5 mM *zinc*. This study suggests that a lower hepatic 5'-deiodinase activity, resulting from a higher *zinc* level, might be related to abnormal energy metabolism in the ob/ob mice.

Zinc can get depleted by high phytates, such as in soy, oats, wheat, or other grains. Rapeseed meal (canola oil is made from rapeseeds) has been shown to reduce thyroid function in experimental animals. The following study shows that zinc supplementation can reverse some of these negative effects from rapeseed.

Title

Beneficial effect of zinc supplementation on reproduction in rats fed rapeseed protein concentrate.

Author

Shah BG; Giroux A; Belonje B; Jones JD

Source

Nutr Metab, 23(4):275-85 1979

Abstract

Three groups of 33 90-day-old female Sprague-Dawley rats were fed, ad libitum, the following diets for 2 weeks before breeding. Diet 1 (D1)

contained 20% protein from casein, diet 2 (D2) had the same level of protein from Tower rapeseed (Brassica napus) protein concentrate (RPC) and diet 3 (D3) was the same as D2 with a zinc supplement (70 mg/l) in the drinking water. From each group 6 animals were killed before breeding and 5-9 animals were killed at 1 and 2 weeks of gestation and post-partum. From each rat, blood, thyroids, liver and femur were collected for the determination of zinc, *copper*, iron, manganese, calcium and magnesium. As a measure of the reproductive performance, body weight, number of pups in the uterus or delivered live or dead, and gestations days before parturition were recorded. The pups were examined for obvious deformities and also analysed for the above mineral elements by atomic absorption spectroscopy. In group D2, levels of zinc in maternal serum, liver, femur and in the pups were significantly lower than the comparable levels in the other two groups. **The zinc supplemented RPC-fed group did not show the anorexia experienced by the unsupplemented group and there was neither a significant difference between reproductive performances of groups D1 and D3 nor was there any significant difference between the zinc levels determined. It was concluded that the toxic symptoms caused by RPC feeding was attributable to zinc deficiency probably caused by the high phytate level in the RPC.**

In the following study zinc was shown to inhibit the T3 binding to rc-erbA beta proteins, indicating "a possible regulatory role for zinc in modulating the intracellular action of thyroid hormone."

Title

Selective effect of zinc compared to other divalent metals on L-triiodothyronine binding to rat c-erbA alpha and beta proteins.

Author

Lu C; Chan JY; Walfish PG

Address

Thyroid Research Laboratory, Samuel Lunenfeld Research Institute of Mt. Sinai Hospital, Canada.

Source

Biochem Int, 21(1):191-8 1990

Abstract

The effects of zinc and other divalent metals on the [125I]T3 binding to rat c-erbA alpha and beta recombinant proteins were assessed. The addition of ZnCl₂ caused a reversible and dose-dependent inhibition of [125I]T3 binding to rc-erbA beta proteins with half maximum inhibition occurring at 50-100 microM, but no significant effect on [125I]T3 binding to rc-erbA alpha under the same assay conditions. Scatchard analysis revealed a decrease in [125I]T3 binding capacity to beta protein without marked change in K_d values in presence of zinc. Moreover, significant inhibitions of [125I]T3 binding to both alpha and beta proteins were observed in the presence of 100 microM of either MnCl₂, CdCl₂ or CuCl₂, but not MgCl₂. Thus, the selective effect of zinc compared to other divalent metals to inhibit T3 binding to rc-erbA beta, but not alpha, proteins was documented and **suggest a possible regulatory role for zinc in modulating the intracellular action of thyroid hormone.**

The following study shows that zinc increases the immune response in calves to sheep red blood cells, offering evidence that zinc is an immune system stimulant.

Title Serum *IgG* and IgM responses to sheep red blood cells (SRBC) in weaned calves fed milk supplemented with Zn and Cu.

Author

Prasad T; Kundu MS

Address

National Dairy Research Institute, Karnal, India.

Source

Nutrition, 11(5 Suppl):712-5 1995 Sep-Oct

Abstract

Because ruminants have a syndesmochorial placenta, the neonates are agammaglobinaemic and prone to morbidity and mortality from opportunistic infections. Only temporary benefit in passive immunity transfer from mother to offspring is derived from feeding colostrum to neonates. The serum immunoglobulin (Ig) G and IgM responses to challenges with sheep red blood cells (SRBC) were investigated in calves fed milk supplemented with zinc, copper, or both. Twenty crossbred calves, weaned on day 5, were divided into four equal groups and fed for 75 d. Group T1 was fed milk alone; group T2 was fed milk supplemented with 25 ppm Cu; group T3 was fed milk supplemented with 100 ppm Zn; and group T4 was fed milk supplemented with 25 ppm Cu and 100 ppm Zn. The antigenic challenges with SRBC were made on days 35 and 65. Serum *IgG* and IgM levels were measured at day 30 and at 2-wk intervals thereafter in collected blood samples. Blood zinc and copper levels and superoxide dismutase (SOD) activity were also measured periodically. **Higher IgG and IgM responses were observed in groups T3 and T4 (the zinc-supplemented groups).** The responses were higher after second challenge with SRBC. The changes in blood copper and zinc concentrations and SOD activity were in accordance with the type of supplementation. **The results suggested that the zinc-supplemented groups in particular showed a stronger humoral immune response, probably as a result of the beneficial effect of zinc on the interaction between T helper cells and B cells.**

The following study investigated the effects of zinc and selenium deficiencies on thyroid hormone metabolism. Both zinc and selenium deficiencies decrease the activity of hepatic type I-5' deiodinase and in this study zinc deficiency caused a bigger decrease than selenium deficiency (but the deficiencies may have been uneven).

There were some interesting differences in the effects on zinc and selenium deficiencies on other thyroid hormone values which may help us to determine deficiencies from thyroid tests. Both zinc and selenium deficiencies decrease T3, but zinc deficiency lowers free thyroxine (fT4) but not T4. Selenium deficiency, on the other hand, lowers T4 but not fT4.

Hypos should pay attention to this. If your T4 is normal but your fT4 is low, then suspect a zinc deficiency. If your fT4 is normal but your T4 is low, suspect a selenium deficiency. This is a good reason to get a

complete thyroid panel done rather than just TSH and T4.

Title

Influence of zinc and selenium deficiency on parameters relating to thyroid hormone metabolism.

Author

Kralik A; Eder K; Kirchgessner M

Address

Institute of Nutrition Physiology, Technical University Munich, Freising-Weihenstephan, Germany.

Source

Horm Metab Res, 28(5):223-6 1996 May

Abstract

48 weaned male Sprague-Dawley rats with an initial average body weight of 41 g were divided into 4 groups of 12 animals (zinc-deficient; zinc-adequate, pair-fed with zinc-deficient group; selenium-deficient; selenium-adequate) for 40 days. All groups were fed a semisynthetic diet with casein being the source of protein. In the selenium-deficient diet, there was a selenium concentration of 0.038 mg/kg. The other diets were supplemented with Na-selenite in order to adjust the selenium concentration to 0.3 mg/kg. In the zinc-deficient diet, there was a zinc concentration of 4.1 mg/kg. The zinc concentrations in the other diets were adjusted to 45 mg/kg by the addition of zinc-sulfate heptahydrate. Zinc-deficient rats were characterized by a markedly reduced alkaline phosphatase activity in their serum, whilst selenium-deficient rats showed a markedly reduced glutathione peroxidase in serum proving their respective zinc-deficient and selenium-deficient states. **Zinc deficiency decreased concentrations of triiodothyronine (T3) and free thyroxine (fT4) in serum by approximately 30% when compared with zinc-adequate controls. The concentration of thyroxine (T4) in serum was not affected by zinc deficiency. Selenium-deficient animals had lower concentrations of T3 and T4 than selenium-adequate animals. The concentration of fT4 in serum was not affected by selenium deficiency. The activity of hepatic type I 5'deiodinase was decreased by 67% by zinc deficiency and by 47% by selenium deficiency compared to adequate controls.** The study data show that both zinc and selenium deficiency affect the metabolism of thyroid hormones.

The following study concludes that excessive zinc "could act as a potential cell toxicant, leading to disturbances in functions of the antioxidant defense system and to alterations in the erythrocyte membrane properties." Increasing the zinc concentration in red blood cells decreases two major antioxidants, catalase and glutathione peroxidase. Glutathione peroxidase is a selenium-based antioxidant so the results suggest that excessive amounts of zinc can deplete selenium. Also depleted by excessive zinc is the red blood cell thiol content. Thiols are sulfur groups which are important in controlling thyroid function. The antithyroid drugs, PTU and Tapazole, work to suppress thyroid function because of their thiol groups.

Title

Zinc-induced damage to carp (*Cyprinus carpio* L.) erythrocytes in vitro.

Author

Akahori A; Gabryelak T; J'ó'zwiak Z; Gondko R

Address

Department of Thermobiology, University of L'ód'z, Poland.

Source

Biochem Mol Biol Int, 47(1):89-98 1999 Jan

Abstract

Fish erythrocytes were used to elucidate the effect of **zinc** ions on the cell antioxidant defence system. **It was detected that an increase of the Zn²⁺ concentration (0.01-1 mM) leads to a marked decrease ($p < 0.05$) in the catalase and the glutathione peroxidase activities.** We observed a loss of 14-39% activity of glutathione peroxidase, and 16-20% diminution for catalase. No significant changes were found in case of the superoxide dismutase. **Incubation of red blood cells with zinc brought about a decrease of the erythrocyte thiol group content.** Treatment of carp erythrocytes with **zinc** ions also resulted in enhanced hemolysis and in the induction of significant ($p < 0.001$) changes in the intracellular glucose level. The increase of glucose concentration in the erythrocytes was correlated with increased concentration of metal in the incubation medium. It was proposed that Zn could affect transport systems across the red blood cells and therefore increased the permeability of the membranes to small molecules (e.g. hexose), and led to hemolysis. **Zinc ions could act as a potential cell toxicant, leading to disturbances in functions of the antioxidant defence system and to alterations in the erythrocyte membrane properties.**

The following study shows that zinc deficiency causes oxidative stress to the retinal metallothionein (MT), the protein which carries zinc and other metals, is protective against lipid peroxidation of retinal membranes. Cadmium (just below zinc in the Periodic Table) is suspected of causing retinal damage and it's possible that a zinc deficiency is a factor in this damage by cadmium. Since I also suspect that cadmium is a major causative factor in thyroid disease and thyroid eye disease, zinc deficiency may be a major factor in both of these conditions.

Title

Zinc deficiency and oxidative stress in the retina of pigmented rats.

Author

Miceli MV; Tate DJ Jr; Alcock NW; Newsome DA

Address

Sensory and Electrophysiology Research Unit, Touro Infirmary, New Orleans, Louisiana 70115, USA.

Source

Invest Ophthalmol Vis Sci, 40(6):1238-44 1999 May

Abstract

PURPOSE: To determine the effect of moderate **zinc** deficiency on antioxidant defenses and measures of oxidative stress in the retina and retinal pigment epithelium (RPE) of Brown Norway Rats. **METHODS:** Twenty-four rats were housed individually and divided into three groups of 8 rats each. Group 1 was fed ad libitum a semipurified control diet formulated to contain 50 parts per million [ppm] total **zinc**; group 2 was fed ad libitum an identical diet but containing 5 ppm total **zinc**; and group 3 was pair-fed the control diet but restricted in amount to that consumed by group 2. Food intake was measured daily and the rats weighed weekly. After 6 weeks, the rats were killed and the following measurements were made: serum **zinc**, serum alkaline phosphatase, retinal zinc, RPE-choroid **zinc**, RPE-choroid catalase, liver metallothionein (MT), retinal MT, RPE-choroid MT, retinal catalase, and retinal thiobarbituric reactive substances (TBARS). **RESULTS:** The following

showed statistically significant differences between groups 2 and 3, respectively: serum Zn (1216 micro/l versus 1555 microg/l, $P \leq 0.01$), serum alkaline phosphatase (3.75 U/mg versus 5.10 U/mg, $P \leq 0.05$), liver MT (4.3 microg/mg protein versus 16.7 microg/mg, $P \leq 0.0001$), RPE-choroid MT (1.3 microg/mg protein versus 2.2 microg/mg, $P \leq 0.02$), retinal MT (0.85 microg/mg protein versus 2.8 microg/mg, $P \leq 0.05$), and retinal TBARS (6.2 nM/mg protein versus 2.2 nM/mg, $P \leq 0.05$). **CONCLUSIONS: The results show that retinal MT and RPE MT concentrations are very sensitive to intake of dietary zinc. The increase in retinal TBARS in group 2 indicates that moderate zinc deficiency increases oxidative stress to the retina. The results also suggest that MT is protective against lipid peroxidation of retinal membranes.**

Histidine is an amino acid involved in protein synthesis. In zinc-deficient rats, histidine incorporation into the protein of skin and muscles is decreased. This may have significance in the effects of zinc deficiency on the health of the skin.

Title

Effect of zinc deficiency on histidine metabolism in rats.

Author

Hsu JM; Rubenstein B

Source

J Nutr, 112(3):461-7 1982 Mar

Abstract

The effects of feeding a diet deficient in zinc (Zn) to male rats on histidine metabolism were studied. Results showed that significantly higher percentages of DL-histidine-carboxyl-14C and L-histidine-2-(ring)-14C were oxidized by Zn-deficient rats. The incorporation of L-histidine-2-(ring)-14C into the proteins of skin, muscle, and kidney were significantly reduced in Zn-deficient rats as compared to Zn-supplemented rats. Conversely, the radioactivity of liver protein of Zn-deficient rats was significantly increased. Zn deficiency increased the activities of liver histidase and urocanase but had no effect on the activity of liver *histidine*-pyruvate transaminase. The increases of enzymatic activities were not due to food intake and can be prevented upon Zn repletion. The liver of Zn-deficient rats contained normal amount of histidine but a reduced quantity of histamine. The results on urinary excretion indicated that Zn-deficient rats discharged the same amounts of one-methyl and three-methyl *histidine* as Zn-supplemented pair-fed rats. Overall findings support in principle the concept that Zn deficiency results in disturbances of protein metabolism and also indicate that Zn is an important factor in regulating histidine metabolism through the urocanic acid pathway.

The following study shows that excess dietary zinc will depress copper levels but excessive copper has little effect on zinc. Copper can ameliorate the toxic effects of excessive zinc including the effects on the blood.

Title

Zinc toxicity, *zinc* deficiency and *zinc*-copper interrelationship in Eimeria acervulina-infected chicks.

Author

Southern LL; Baker DH

Source

J Nutr, 113(3):688-96 1983 Mar

Abstract

Three experiments were conducted with young chicks to investigate the effect of duodenal coccidiosis caused by Eimeria acervulina infection on Zn toxicity, Zn deficiency and the interrelationship between Zn and Cu. The coccidial infection depressed both rate and efficiency of weight gain. Dietary Zn addition at 2000 mg/kg depressed performance only slightly, but the 4000 mg/kg reduced both gain and gain/feed markedly. The coccidial infection appeared to have an ameliorative effect on Zn toxicity as assessed by performance and by hematological parameters. Excess Zn (2000 and 4000 mg/kg) dramatically increased liver, pancreas and bone Zn levels. The coccidial infection, however, decreased tissue Zn levels. Copper toxicity caused by feeding 500 mg Cu per kilogram diet was exacerbated by E. acervulina infection. **A Zn-Cu antagonism was observed in both control and in coccidiosis-infected chicks. Excess dietary Zn decreased tissue Cu deposition, but excess Cu did not affect tissue Zn deposition. Copper partially ameliorated Zn toxicity symptoms. The efficacy of Cu in overcoming the Zn-induced depressed hematological parameters, however, was enhanced slightly by coccidiosis. E. acervulina infection did not affect the chick's Zn requirement. Growth data were more reliable as indicators of the Zn requirement than were blood or bone parameters.**

Although consequences of *zinc* deficiency have been recognized for many years, it is only recently that attention has been directed to the potential consequences of excessive *zinc* intake. This is a review of the literature on manifestations of toxicity at several levels of *zinc* intake. *Zinc* is considered to be relatively nontoxic, particularly if taken orally. However, manifestations of overt toxicity symptoms (nausea, vomiting, epigastric pain, lethargy, and fatigue) will occur with extremely high *zinc* intakes. At low intakes, but at amounts well in excess of the Recommended Dietary Allowance (RDA) (100-300 mg Zn/d vs an RDA of 15 mg Zn/d), evidence of induced copper deficiency with attendant symptoms of anemia and neutropenia, as well as impaired immune function and adverse effects on the ratio of low-density-lipoprotein to high-density-lipoprotein (LDL/HDL) cholesterol have been reported. Even lower levels of *zinc* supplementation, closer in amount to the RDA, have been suggested to interfere with the utilization of copper and iron and to adversely affect HDL cholesterol concentrations. Individuals using *zinc* supplements should be aware of the possible complications attendant to their use [zinc toxicity.doc](#)

Mechanisms of *zinc* (Zn) toxicity are incompletely understood and data regarding potential endocrine alterations in Zn toxicity are scarce. To examine mechanisms of Zn toxicity, day-old chicks were pair-fed diets containing 5280 ppm (Hz) or 73 ppm (CON) Zn. Impaired postnatal growth, independent of feed consumption, and multiple endocrinopathies were observed following short-term (1-2 weeks) exposure to the high Zn diet. Reduced levels of serum cholesterol, high-density lipoprotein cholesterol, and growth hormone were associated with HZ feeding. Depressed levels of circulating thyroid hormones and histological evidence that follicle area of thyroids from HZ birds was 63% less than CON indicated that impaired growth of HZ birds may be caused, in part, by reduced thyroidal function. [zinc toxicity effect on thyroid in chicks.doc](#)

The present study indicates that germanium and selenium disturbs bone metabolism in weanling rats, and that this disturbance is reversed by

The tumour-localizing abilities of various kinds of porphyrin derivatives in tumour-bearing hamsters were assessed by nitrogen-pulsed laser spectrofluorometry (N2-PLS). On examination of porphine derivatives (from haemoglobin), it was found that the dimer and acetylated and amidated compounds had a high affinity for tumour tissue; the dimer and hydroxylated compound of phorbine derivatives (from chlorophyll) also showed a high affinity. Furthermore, of the metalloporphyrins (gallium, **zinc** and indium complexes), those which contained hydrophilic groups showed a high affinity for tumour tissue; of the metallophorbines (gallium, **zinc** and indium complexes), those which contained hydrophobic groups showed a high affinity. A correlation was found between the side-chain structure of the porphyrins and metalloporphyrins and their affinity for tumour tissue. [gallium and porphyrins.doc](#)

Thus, the selective effect of zinc compared to other divalent metals to inhibit T3 binding to rc-erbA beta, but not alpha, proteins was documented and suggest a possible regulatory role for zinc in modulating the intracellular action of thyroid hormone. [zinc regulates intracellular action of thyroid hormone.doc](#)

"Zinc Fingers", Daniela Rhodes and Aaron Klug, Scientific American, February 1993

"They play a key part in regulating the activity of genes in many species, from yeasts to humans. Ten years ago, no one knew they existed."

Synopsis: This is one of the most significant discoveries of this decade, and applies directly, and powerfully, to the crucially vital roles of the trace elements in our daily nutrition. Since this landmark article does not contain any short, descriptive passages suitable for quoting, this synopsis will have to do.

In order to translate the genetic information in our DNA into amino acids, proteins, messenger RNA, and RNA, certain molecules are required which can read-out the information stored in specific stretches of our DNA. These very specific DNA-reading "transcription factor" molecules can have anywhere from two to 29 "fingers" which fit, like a sophisticated key into a high-precision lock, into highly specific stretches of our DNA.

Transcription factors are made from long strings of amino acids, which are folded into highly specific shapes with many "fingers" - somewhat like we fold a ribbon into loops (or "fingers") to make a Christmas bow.

Now then, and this is the crucial part of the authors' discovery. The 'glue' which forms the straight ribbon of amino acids into finger-like loops is an atom of zinc, at the base of every "finger".

Comments: The conclusions are stunning, powerful, and far-reaching. If there happens to be a zinc deficiency in the organism, the "fingers" of the transcription factors cannot be formed, and although all the genetic information is there, it cannot be transcribed, and used by the organism - be this a yeast cell, a frog, a mouse, or a human. Consequently, the organism will be defective, and its metabolism and immune functions will be severely compromised.

This is the first discovery that the trace elements - there are undoubtedly others than zinc as well - perform a profoundly vital function right at the genetic base of our existence. Hence, the consequences of a zinc deficiency will be very wide-ranging - from many kinds of birth defects to compromised and abnormal metabolic, endocrine and immune functions. Worse, and because of this, a zinc deficiency in the mother can result in faulty genes in her children, due to the sabotaged transcription of her DNA into her offspring's DNA. These children with faulty genes will then pass on their genetic defects to their subsequent offspring and following generations! [zinc fingers.doc](#)

Effects on the tissue mineral concentrations of pigs from sows fed four dietary Zn levels were studied. A male and a female from first- and second-parity litters were killed at 1 and 21 d of age. The dams were fed a corn-soybean meal basal diet supplemented with 0, 50, 500 or 5,000 ppm Zn from 30 kg body weight until completion of the second lactation. Pigs from sows fed 5,000 ppm additional zinc had heavier liver, heart, thyroid and adrenal weights relative to their body weight than did pigs from sows on the other treatments. First- and second-parity pigs from sows on the highest Zn supplementation level had higher Fe stores in the liver, higher Zn concentrations in the liver, kidney and pancreas, and higher Cu levels in the kidney compared with pigs from sows on the other treatments. However, Cu concentrations in the liver, heart, pancreas, esophagus, aorta and testes were reduced in pigs from sows on the 5,000 ppm Zn treatment. In first-parity pigs, Ca in the liver was higher for pigs whose dams received 5,000 ppm Zn compared with pigs from sows on all other treatments, and the Mn level was higher compared with pigs from sows receiving 50 or 500 ppm additional zinc. Pigs at 1 d of age from sows on the 0, 50 or 500 ppm treatment had lower hepatic P and Zn concentrations than pigs from sows on the same treatment at 21 d of age. The reverse was true for pigs whose dams received 5,000 ppm Zn. [zinc-effects on different mineral concentrations.doc](#)

Zinc deficiency was produced experimentally in guinea-pigs fed on a diet containing 1.03 mg Zn/kg over a period of 45 days. Clinical signs exhibited in Zn-deficient (ZnD) animals were depression with abnormal posture, scaly skin lesions on various parts of the body, oedematous swelling on hind limbs and marked alopecia. There was no effect on food intake. Serum studies in ZnD group revealed significant decreases in the concentrations of Zn from 20 days onwards, and tri-iodo-thyronine (T3) and thyroxine (T4) from 30 days onwards. Thyroid glands of ZnD animals were smaller in size and pale or whitish pale in colour. Histopathologically, these glands showed changes of atrophy and degeneration in the follicles. It could be concluded that the depletion in serum T3 and T4 due to Zn deficiency was related to thyroid lesions. [zinc deficiency effects on thyroid in guinea-pigs.doc](#)

Thanks to progress in zinc research, it is now possible to describe in more detail how zinc ions (Zn⁺⁺) and nitrogen monoxide (NO), together with glutathione (GSH) and its oxidized form, GSSG, help to regulate immune responses to antigens. NO appears to be able to liberate Zn⁺⁺ from metallothionein (MT), an intracellular storage molecule for metal ions such as zinc (Zn⁺⁺) and copper (Cu⁺⁺). Both Zn⁺⁺ and Cu⁺⁺ show a concentration-dependent inactivation of a protease essential for the proliferation of the AIDS virus HIV-1, while zinc can help prevent diabetes complications through its intracellular activation of the enzyme sorbitol dehydrogenase (SDH). A Zn⁺⁺ deficiency can lead to a premature transition from efficient Th1-dependent cellular antiviral immune functions to Th2-dependent humoral immune functions. Deficiencies of Zn⁺⁺, NO and/or GSH shift the Th1/Th2 balance towards Th2, as do deficiencies of any of the essential nutrients (ENs) - a group that includes methionine, cysteine, arginine, vitamins A, B, C and E, zinc and selenium (Se) - because these are necessary for the synthesis and maintenance of sufficient amounts of GSH, MT and NO. Via the Th1/Th2 balance, Zn⁺⁺, NO, MT and GSH collectively determine the progress and outcome of many diseases. Disregulation of the Th1/Th2 balance is responsible for autoimmune disorders such as diabetes mellitus. Under Th2, levels of interleukin-4 (IL-4), IL-6, IL-10, leukotriene B4 (LTB4) and prostaglandin E2 (PGE2) are raised, while levels of IL-2, Zn⁺⁺, NO and other substances are lowered. This makes things easier for viruses like HIV-1 which multiply in Th2 cells but rarely, if ever, in Th1 cells. AIDS viruses (HIVs) enter immune cells with the aid of the CD4 cell surface receptor in combination with a number of co-receptors which include CCR3, CCR5 and CXCR4. Remarkably, the cell surface receptor for LTB4 (BLTR) also seems to act as a co-receptor for CD4, which helps HIVs to infect immune cells. The Th2 cytokine IL-4 increases the number of CXCR4 and BLTR co-receptors, as a result of which, under Th2, the HIV strains that infect immune cells are precisely those that are best able to accelerate the AIDS disease process. The IL-4 released under Th2 therefore not only promotes the production of more HIVs and the rate at which they infect immune cells, it also stimulates selection for the more virulent strains. Zn⁺⁺ inhibit LTB4 production and numbers of LTB4 receptors (BLTRs) in a concentration-dependent way. Zn⁺⁺ help cells to keep their LTB4 'doors' shut against the more virulent strains of HIV. Moreover, a sufficiency of Zn⁺⁺ and NO prevents a shift of the Th1/Th2 balance towards Th2 and thereby slows the proliferation of HIV, which it also does

by inactivating the HIV protease. Research makes it look likely that deficiencies of ENs such as zinc promote the proliferation of Th2 cells at the expense of Th1 cells. Zinc deficiency also promotes cancer. Under the influence of Th1 cells, zinc inhibits the growth of tumours by activating the endogenous tumour-suppressor endostatin, which inhibits angiogenesis. The modern Western diet, with its excess of refined products such as sugar, alcohol and fats, often contains, per calorie, a deficiency of ENs such as zinc, selenium and vitamins A, B, C and E, which results in disturbed immune functions, a shifted Th1/Th2 balance, chronic (viral) infections, obesity, atherosclerosis, autoimmunity, allergies and cancer. In view of this, an optimization of dietary composition would seem to give the best chance of beating (viral) epidemics and common (chronic) diseases at a realistic price.[zinc what.doc](#)

We have previously reported in patients with hyperthyroidism that the red blood cell (RBC) zinc (Zn) concentration reflects the mean thyroid hormone concentration over the preceding months. In the present study, the concentration of RBC Zn was measured by a simple and easy method with a Zn-test Wako kit. Within-run and between-run precision were 1.4% and 1.3%, respectively. The relationship between RBC concentration and dilution was linear. The average recovery was 103%. A good correlation ($r=0.97$) was obtained between this method and atomic absorption spectrophotometry. The mean concentration of RBC Zn in 39 euthyroid controls was 12.6 ± 1.3 mg/l, ranging from 10.4 to 15.1 mg/l. The RBC Zn concentrations in 38 patients with Graves' disease, in 10 patients with silent thyroiditis and in 3 patients with gestational thyrotoxicosis were 7.3 ± 1.6 (3.2-9.8), 12.0 ± 1.6 (9.5-14.2) and 11.8 ± 1.7 (10.5-13.7) mg/l, respectively. The concentration of RBC Zn was able to differentiate hyperthyroid Graves' disease from transient thyrotoxicosis except in 1 case and was a better index than TSH-binding inhibitory immunoglobulin. These results indicate that measuring RBC Zn with the Zinc-test Wako kit is very useful in differentiating hyperthyroid Graves' disease from transient thyrotoxicosis.[zinc levels in RBC and Grave's disease.doc](#)

In this study, experimental hyperthyroidism was established and used to investigate possible alterations in the calcium (Ca), magnesium (Mg), and zinc (Zn) homeostasis by assessing their concentrations in plasma and erythrocytes. In the L-thyroxine-induced hyperthyroidism condition, the experimental animals show a significant decrease in erythrocyte Ca, Mg, and Zn concentrations, and a significant decrease in plasma Mg concentration. Significant positive correlations were found for Mg and Zn both in plasma and in erythrocytes. The results suggest that the homeostasis of Ca, Mg, and Zn is altered during experimental hyperthyroidism.[zinc and magnesium levels correlate in hyperT.doc](#)

The following study shows that zinc is higher in the red blood cells in hyperthyroidism.

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Elements in erythrocytes of population with different thyroid hormone status.

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The contents of elements K, Ca, Fe, Cu, Zn, Se, and Rb in erythrocytes of 78 cases with different thyroid hormone status have been measured by proton-induced X-ray emission and neutron activation analysis. According to the status of thyroid hormones T3, T4, TSH, FT3, and FT4 detected by radioimmunoassay, the experiment subjects were divided into four groups (i.e., hyperthyroid, hypothyroid, critical [one of thyroid hormones was abnormal], and normal). Elements contents and hormones levels of four groups were analyzed by one-way analysis of variance and correlation using an SPSS/PC statistical package. The results showed that the Se contents of four groups were not significantly different ($p<0.05$). Zn content of hypothyroid group was significantly higher than those of hyperthyroid and critical groups. **The Zn content of the normal group was higher than that of the hypothyroid group and lower than that of the hyperthyroid and critical groups.** In the hyperthyroid group, there were significant correlations between elements contents and thyroid hormones levels (except TSH), but not between elements contents and levels of thyroid hormones. **However, in the hypothyroid group, relatively strong correlations have been found between elements contents and thyroid hormones levels, especially between Zn and the T3/T4 ratio, and between Zn and TSH.**

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